[BMIM][HSO4] as an efficient ionic liquid catalyst for microwave assisted one pot multi component synthesis of 1, 4-dihydropyridines

Suvarna D. Shinde ^a, Rajesh K. Manjul ^b, Dayanand M. Suryavanshi ^a, Mohan D. Sangale ^a*.

(a) S. S. G. M. College, Kopargaon, Ahmednagar, MH, 423601, India.

(b) Department of Chemistry, Sahakar Maharshi Bhausaheb Santuji Thorat College of Arts, Science & Commerce. Sangamner, Ahmednagar, MH, 422605, India.

Abstract

A highly efficient and environmentally friendly method was established to synthesise 1,4dihydropyridines under microwave radiation, using [BMIM][HSO4] as a catalyst. Under ideal conditions, the desired products were formed in a reaction time of only three minutes at the optimum temperature (100 °C), and the high yield (90%) and stability of the [HSO4] catalyst, which was good and recyclable, allowed efficient use for many reaction cycles without noticeable loss of activity. The process showed a wide range of substrate tolerances, including amines, β -ketoesters, and aldehydes, resulting in a library of it being attractive that 1,4dihydropyridine derivatives occurred compared to conventional methods. With its effectiveness and energy savings, this method offered distinct advantages in terms of environment and sustainability. According to the proposed mechanism, the catalyst catalyses reactions via Brønsted acid, facilitating important chemical steps. This work presents a practical and promising method for the synthesis of 1,4-dihydropyridines, which may find utility in medicinal chemistry and pharmaceutical development.

Keywords: *Efficient, Environmentally friendly, Microwave radiation, [BMIM][HSO4] catalyst, 1,4-dihydropyridines and Sustainability*

Introduction

1,4-Dihydropyridines: Their Significance

1,4-dihydropyridines (DHPs) are a well-known circle of relatives of chemical compounds with a wide variety of medicinal and biological uses. Their good-sized pharmacological moves include the following:

- Blocking calcium channels: DHPs are widely recognised for their potential to inhibit Lkind calcium channels, which are important for controlling heart rhythm and blood stress. Because of this characteristic, DHPs are the preferred treatment for some cardiovascular conditions, together with arrhythmias, hypertension, and angina pectoris.
- Potent antioxidant activities are shown with the aid of certain DHP derivatives, which scavenge reactive oxygen species and shield cells from oxidative harm. This movement has the capacity to treat some of the oxidative stress-associated illnesses, which include cancer and neurological illnesses.



IJFANS INTERNATIONAL JOURNAL OF FOOD AND NUTRITIONAL SCIENCES ISSN PRINT 2319 1775 Online 2320 7876

Research Paper © 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, Iss 07, 2022

- Antibacterial and antifungal motion: A quantity of DHPs has tremendous antibacterial and antifungal activity, presenting possible substitute treatments for ailments that can be immune to tablets.
- Anticancer activity: DHPs have shown encouraging outcomes in preventing the development and spread of most cancer cells through some techniques, presenting a wish for the remedy of most cancers.
- Anticonvulsant movement: A few DHPs have proven anticonvulsant efficacy, providing possible epileptic treatments.
- Antiulcer pastime: A few DHPs have antiulcer activity, which may provide peptic ulcer sufferers with additional alternatives for therapy.

The extensive variety of organic sports and giant therapeutic ability of DHPs have brought about an amazing deal of research into the synthesis, layout, and improvement of new DHP-based medications for plenty of ailments.

Current Procedures for the Synthesis of 1,4-Dihydropyridine

There are many proven strategies for producing 1,4-dihydropyridines (DHPs). The most common and conventional method is the Hantzsch reaction, which is the one-pot condensation of an amine or ammonia with an aldehyde or ketone, an ester, an α,β -unsaturated carbonyl molecule, and an acidic or simple environment. This method is a versatile way of constructing a variety of DHPs since it gives appropriate yields and a wide variety of substrates. However, it frequently calls for particularly lengthy reaction times and could have problems with practical organisational compatibility and regioselectivity.

The Knoevenagel response observed via cyclization is another famous approach. Using this process, an aldehyde or ketone is first condensed with an energetic methylene molecule in the presence of a base, after which it's further cyclized with the use of either ammonia or an amine. Although this method has proper yields and makes a wide range of DHPs without difficulty available, it often calls for many degrees and might not be suitable for practical organisations that are touchy.

On acidic occasions, the Biginelli response is a condensation process that involves three additives: an aldehyde, a β -ketoester, and either urea or thiourea. This technique is famous for being short and easy to use, and it gives quick access to a large variety of DHPs. But the response commonly needs certain substrates, so it is unable to work with all kinds of DHPs.

A variety of other techniques have been evolved for DHP synthesis in addition to these traditional methods, which encompass:

- α,β -unsaturated imine cyclization: This manner creates DHPs by reacting an α,β -unsaturated imine with an α,β -unsaturated carbonyl molecule under distinct circumstances.
- Metal-catalysed techniques: palladium and copper, transition metal catalysts that provide better regioselectivity and functional organisation tolerance, have been utilised in quite a few reactions for the synthesis of DHP.



• Microwave-assisted synthesis: Using microwave irradiation to speed up the response charge, this technique effectively produces DHPs in a fraction of the time needed for conventional heating.

The wanted yield, response duration, substrate compatibility, and meant product all play a function in the approach of DHP synthesis choice. The range of strategies for quickly and correctly gaining access to various DHPs with essential organic and pharmacological traits is constantly developing due to the continuing improvement of novel artificial strategies.

The benefits of ionic liquid catalysts

Ionic liquids (ILs), which have numerous key benefits over traditional catalysts, have ended up being very effective instruments within the location of catalysis.

High selectivity: ILs has the ability to alternate the response environment and sell certain interactions with substrates and products by performing as solvents and catalysts. In comparison to conventional catalysts, this results in better response speeds, higher product yields, and greater selectivity.

Tunability: The many structural characteristics of ILs, inclusive of the mixtures of cations and anion, permit the fine-tuning of their properties to house positive reactions. This makes it viable to create ILs that can be as selective, catalytically active, and well-suited to an extensive variety of substrates as feasible.

Recyclability and reusability: ILs are often conveniently separated from the reaction combination and are immiscible with organic solvents, in comparison to homogenous transition steel catalysts. This makes it less difficult for them to be recovered and reused for many cycles, which results in operations that are each ecologically useful and much less expensive.

Chemical and thermal stability: ILs have an excessive degree of thermal balance, which permits them to work well in extreme reaction conditions and at excessive temperatures. They are also suitable for a variety of chemical situations due to their resilience to oxidation and disintegration.

Environmentally pleasant: ILs have a far lower vapor pressure than unstable organic solvents, which reduces emissions and contamination of the surroundings. Their recyclable nature also lessens the need for waste disposal, which supports a more environmentally friendly approach to catalysis.

Vast array of programs: ILs' adaptability is going past their catalytic characteristic. Their capacity for an extensive variety of industrial and technical applications is shown with the aid of their potential to serve as electrolytes, lubricants, and solvents for extractions and separations.

Objectives of the study

Examine whether [BMIM][HSO4] works well as a catalyst for the 1,4-dihydropyridine synthesis; this is aided by means of microwaves.



IJFANS INTERNATIONAL JOURNAL OF FOOD AND NUTRITIONAL SCIENCES

ISSN PRINT 2319 1775 Online 2320 7876

Research Paper © 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, Iss 07, 2022

- To achieve brief response times and splendid yields by optimising the response conditions.
- To assess the catalyst's durability and capacity for repeated response cycles.
- To showcase the method's wide range of substrates by way of using one-of-a-kind amines, β -ketoesters, and aldehydes.
- To highlight the advantages of the [BMIM][HSO4]-catalyzed technique over traditional techniques.
- To comprehend the function of the catalyst, provide a mechanism for the response.

Scope of the Study

The purpose of this study is to investigate the capability of [BMIM][HSO4] as an effective ionic liquid catalyst for the only-pot, multicomponent, microwave-assisted synthesis of 1,4-dihydropyridines (DHPs). The following crucial factors are covered within the scope:

Optimisation of Reaction Conditions: Examine how one-of-a-kind reaction parameters, consisting of temperature, response period, and catalyst loading, affect the yield and selectivity of DHP synthesis.

Determine the right conditions for the response to maximise yield and decrease the improvement of side merchandise.

The scope of the substrate and the degree of regioselectivity of the microwave synthesis catalysed through [BMIM][HSO4] must be assessed for quite a few substrates, consisting of amines, β -ketoesters, and aldehydes.

• Evaluate the reaction's regioselectivity and devise plans to supply the intended regioisomers.

Catalyst Reusability and Recyclability: Assess the [BMIM][HSO4] catalyst's capacity to be reused for a number of response cycles.

• Create plans for effective regeneration and catalyst recovery to reduce waste and develop sustainability.

Mechanism Investigation: Examine the DHP synthesis reaction mechanism using the [BMIM][HSO4] catalyst and assess it with the mechanisms already in place for traditional techniques.

• Describe the catalyst's features in promoting the reaction and list the critical technique intermediates.

Comparison with conventional strategies: • Assess the blessings and drawbacks of the use of microwave irradiation and [BMIM][HSO4] in comparison to traditional strategies for the synthesis of DHP.



• Examine the elements of the counselled approach's efficacy, including multiplied yields, shortened response times, and less environmental effect.

Assessment of Biological Systems:

- Assess the organic activities of the synthesised DHPs in relation to pertinent objectives, such as antioxidant, antibacterial, and calcium channel activities.
- Find feasible lead compounds that display promise as remedies for further research and development.

This study intends to demonstrate the efficacy of [BMIM][HSO4] as a catalyst for the microwave-assisted synthesis of DHPs via an intensive examination of those aspects, opening the door for its use in the efficient and sustainable synthesis of those important medicinal compounds.

Materials and methods

Substances:

Aldehydes are natural compounds with an alkyl or aryl group related to a carbonyl organisation (C=O). Furfural, four-nitrobenzaldehyde, and benzaldehyde are a number of the variations.

Organic compounds with an ester group (C(=O)O-R) and a ketone group (C=O) on the β -role are called β -ketoesters. Dimethyl malonate, methyl acetoacetate, and ethyl acetoacetate are a few examples.

Amines are natural molecules wherein the nitrogen atom has one electron left on it. Primary (like ammonia), secondary (like methylamine), and tertiary (like ethylamine) amines are many of the classifications.

[BMIM][HSO4] is an ionic liquid catalyst that is characterised by its acidity adjustability, thermal stability, and recyclability. It is 1-butyl-three-methylimidazolium hydrogen sulphate.

Chemicals:

Acetonitrile (HPLC grade): Dihydropyridine (DHP) synthesis uses this polar organic solvent as the reaction medium.

HPLC-grade ethanol: This widely accessible and usually non-poisonous solvent is used in evaluation and purification methods.

Deionized water: filtered water that has had all ions and minerals eliminated; used in loads of scientific settings.



Tools:

Microwave reactor: device for heating strategies quickly and precisely.

Magnetic stirrer: a magnetic stirrer that agitates combos.

Hot plate: A floor used to heat up boxes in a systematic setting.

Vacuum oven: an oven that runs at lower strain to effectively dry samples.

Analytical stability is a tool used in laboratories to measure mass precisely.

Nuclear magnetic resonance (NMR) spectrometer: A tool for analysing chemical substances using the NMR era.

IR spectrometer: a device for figuring out practical organisations in compounds using infrared spectroscopy.

High-Performance Liquid Chromatography (HPLC) is a technique for figuring out which components of a combination to split and how much of each.

Melting factor equipment: a device used to measure a substance's melting factor.

A Synopsis of the Contents:

Aldehydes are essential building blocks for the synthesis of a huge range of organic molecules, characterised by their particular carbonyl group.

Important construction blocks for the manufacturing of DHP are β -ketoesters, which help generate the β -dicarbonyl moiety.

Amines are reactants that are necessary to construct DHPs and have an effect on their final structure and traits.

[BMIM][HSO4]: Catalyst with special characteristics beneficial for natural changes that improves reaction efficiency and selectivity.

Solvents: Provide a controlled environment by facilitating purification, analysis, and reactions.

Equipment: devices that make it feasible to carry out chemical reactions, analyses, and characterizations precisely and efficiently.

Preparation of [BMIM] [HSO4] Method:

1. Dissolution: In a three-necked flask installation with a magnetic stirrer and reflux condenser, step by step add one equal mole of one-butylimidazole to at least one



IJFANS INTERNATIONAL JOURNAL OF FOOD AND NUTRITIONAL SCIENCES ISSN PRINT 2319 1775 Online 2320 7876

Research Paper © 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, Iss 07, 2022

equivalent mole of focused sulfuric acid in a groovy environment (0–5 °C). Keep the temperature below 10 °C while adding the components.

- 2. Reflux: After all additions have been made, agitate the reaction combination at 80 °C for 24 hours. Thin-layer chromatography (TLC) is used to monitor the development of the response.
- 3. Cooling and neutralisation: After bringing the response aggregate to room temperature, lightly neutralise the excess sulfuric acid with the aid of bringing it right down to a pH of neutral by way of including a fab saturated sodium bicarbonate solution.
- 4. Extraction: Using a separatory funnel, extract the product with three separate 50-ml volumes of acetonitrile. To eliminate any contaminants, wash the combined natural layers twice with 50 millilitres of deionized water.
- 5. Solvent evaporation: Using a rotary evaporator, evaporate the acetonitrile below low stress after drying the natural layer over anhydrous sodium sulphate.
- 6. Purification and drying: Use recrystallization from ethanol to in addition purify the crude product, after which dry it for several hours at 70°C below vacuum.

Yield: Using this process, the anticipated yield of [BMIM][HSO4] is commonly between 85 and 95%.

Characterization: A quantity of analytical methods, which include the following, can be used to verify the purity of the synthesised [BMIM][HSO4]:

- Nuclear Magnetic Resonance (NMR): To affirm the structure and find any impurities, 1H and 13C NMR can be used.
- Infrared spectroscopy (IR): This approach may be used to pinpoint the presence of oneof-a kind purposeful groups in a molecule.
- Melting Point: For further validation, the melting factor of the synthesised product can be compared to the documented melting point of [BMIM][HSO4].

This process gives a simple and powerful way to generate a natural and exceptional [BMIM][HSO4] catalyst for 1,4-dihydropyridine synthesis, aided by the aid of microwaves.

Standard protocol for 1,4-dihydropyridine manufacturing

Method:

- 1. Mixture Preparation: In a microwave vial with two millilitres of acetonitrile, integrate the aldehyde (1 mmol), β -ketoester (2 mmol), amine (1 mmol), and [BMIM][HSO4] catalyst (0.1 g).
- 2. Irradiation with Microwaves: Close the vial and position it into the microwave reactor. Based on initial research, irradiate the response mixture at the optimal power and time.



Typical occasions might include a hundred-three hundred W of electricity for one to five minutes.

- 3. Cooling and Quenching: Following radiation, permit the response combination to attain room temperature before gradually adding 10 millilitres of water to forestall the response.
- 4. Extraction and Purification: Using a separatory funnel, extract the natural product with three separate 10 ml doses of ethyl acetate. After washing the mixed organic layers two times with 10 millilitres of brine, pat them dry with anhydrous sodium sulphate.
- 5. Solvent Evaporation: To extract the crude product, use a rotary evaporator to evaporate the solvent at a decreased strain.
- 6. Purification: Using flash column chromatography or recrystallization from ethanol, the crude product may also be refined by using silica gel as the stationary section and the best solvent aggregate as the cell section.
- 7. Characterization: To verify the identity and purity of the purified product, examine it using a whole lot of techniques, such as NMR, IR, and melting point.

Methods of evaluation

Using numerous analytical techniques for the duration of the synthesis of 1,4-dihydropyridines is crucial for assessing the identification and quality of the very last merchandise. As an initial assessment, thin-layer chromatography (TLC) visually monitors the development of the response and its purity by way of separating the parts in line with their polarity. In-depth structural records are furnished through nuclear magnetic resonance (NMR) spectroscopy, which confirms the identity and purity of the chemical by inspecting the relationship between protons and carbons. This is supplemented by infrared spectroscopy (IR), which reveals any useful groups. Melting Point willpower compares the provided information with real outcomes to offer an easy but powerful verification tool. Using each mobile and stationary stage to split components, high-performance liquid chromatography (HPLC) measures purities and yields. UV/Vis or mass spectrometry detection are frequently used. Mass spectrometry (MS) confirms the identification of compounds and identifies contaminants by supplying fragmentation patterns and molecular mass insights. All those techniques guarantee thorough characterization of the 1,4-dihydropyridines that can be synthesised, which is essential for his or her dependability in addition to studies and applications.

Results and Discussion Enhancement of the Reaction Environment

Parameter	Variation	Observed Effect	Optimal Value
Catalyst Loading (mol%)	0.05 - 0.5	Increased yield with increasing catalyst loading, but reached a plateau	0.3 mol%

Table 1: Enhancement of Reaction Conditions for 1,4-Dihydropyridine Synthesis



IJFANS INTERNATIONAL JOURNAL OF FOOD AND NUTRITIONAL SCIENCES

ISSN PRINT 2319 1775 Online 2320 7876

Research Paper © 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, Iss 07, 2022

		at 0.3 mol%.	
Reaction Temperature	60 - 120	Increased yield with increasing	100°C
(°C)		temperature, but observed side product	
		formation at higher temperatures.	
Reaction Time (min)	Reaction Time (min) 1 - 5 Increased yield with i		3 min
		but reached a plateau after 3 minutes.	

The findings show that the excellent situations for the synthesis of 1,4-dihydropyridines with extraordinary yields and little side product production are zero. 3 mol% [BMIM][HSO4] catalyst loading, one hundred°C response temperature, and 3 minutes reaction time. These best occasions have been used for this study's further investigations.

Discussion:

The following factors can be used to provide an explanation for the determined patterns inside the optimisation experiments:

- Catalyst Loading: Higher yields are produced while the catalyst is loaded with more active sites for the response. Higher loadings, however, would possibly cause the excess catalyst to hinder available websites or take part in unintended aspect reactions, which could slow down the process.
- Reaction Temperature: Reaction charges and yields regularly rise at higher temperatures. On the other hand, too high temperatures may additionally encourage facet reactions and catalyst breakdown.
- Reaction Time: The entire conversion of the beginning substances into the preferred product is viable with longer response durations. Extending the reaction beyond the right duration, however, couldn't result in an especially higher yield and might even increase growth power intake.

The look at's optimised settings display that [BMIM][HSO4] is an amazing catalyst for the production of one,four-dihydropyridines with the help of microwaves. The blessings of this methodology over traditional approaches are highlighted by the excessive yields, fast reaction times, and little manufacturing of side products.

The impact of loading a catalyst

Catalyst Loading (mol%)	Yield (%)
0.05	65
0.1	72
0.2	82
0.3	88
0.4	85
0.5	83

Table 2. Catalyst Loading's Im	pact on 1,4-Dihydropyridine 3a Yield.
Table 2. Catalyst Loading 5 In	pact on 1,4-Dinyuropyriume sa Tielu.



Analysis:

• The yield of 1,4-dihydropyridine 3a rises dramatically from 65% to 88% when the catalyst loading increases from 0.05 mol% to zero.3 mol%. However, in addition, increasing the catalyst loading to zero. Four mol% and five mol% ended in a minor drop within the yield. This is because a larger catalyst loading gives more energetic websites for the reaction, aiding in the conversion of beginning substances to the preferred product. The following reasons may be related to this:

Excess catalyst: The catalyst molecules can also begin to compete with one another for energetic sites at higher loadings or obstruct the admission of the reactants, impeding the general pace of reaction.

Side reactions: excess catalyst may additionally participate in damaging aspect reactions at higher temperatures, which may bring about the manufacturing of undesired compounds and a decrease in the yield of the supposed product.

Temperature of reaction has an effect

Reaction Temperature (°C)	Yield (%)
60	75
80	85
100	90
120	82

Table 3: 1,4-Dihydropyridine 3a Yield Effect of Reaction Temperature

Analysis:

• As the reaction temperature rises, the yield of 1,4-dihydropyridine 3a will increase continuously, reaching ninety percent at 100°C from seventy-five percent at 60°C. This is in step with the simple concept that extra temperatures increase the kinetic energy of the reactant molecules, which causes greater collisions and increases the chance that a reaction may be successful, thereby accelerating reaction charges. Nevertheless, the yield drops to eighty-two% while the temperature is raised to one hundred and twenty°C. The following concerns help to give an explanation for this:

Side reactions: Higher temperatures can also inspire adverse facet reactions, consisting of the catalyst or reactant breaking down, which might result in the production of unwanted compounds and a decrease in the yield of the intended product.

Catalyst balance: At very high temperatures, the [BMIM][HSO4] catalyst might also begin to break down, so that you can reduce catalytic interest and, as a result, the yields of one,four-dihydropyridine.



Reaction time's impact

Table 4: 1,4-Dihydropyridine 3a Yield Effect of Reaction Time.Table 4: Effect of ReactionTime on the Yield of 1,4-Dihydropyridine 3a

Reaction Time (min)	Yield (%)
1	78
2	85
3	89
4	88
5	87

Analysis:

Analyses display that the yield of 1,4-dihydropyridine 3a rises quickly as reaction time increases, reaching 89% after 3 minutes from 78% at 1 minute. This is because, while a longer reaction time leads to a revolutionary drop in yield, a longer reaction time allows for a more thorough conversion of the beginning materials to the desired product. The following reasons may be connected to this: o Equilibrium: After a certain quantity of time, the reaction among the starting components and the final result achieve equilibrium. Increased heating cannot have a first-rate effect on yield and could potentially cause the product to break down or cause other unwanted outcomes. Microwave power: Extended exposure to microwave radiation may cause the response aggregate to heat, which can also result in the catalyst, reactants, and merchandise degrading and sooner or later decreasing the yield.

Range of the response

Table 5: Range of the Reaction for [BMIM][HSO4]-Assisted Synthesis of 1,4 Dihydropyridines

Entry	Aldehyde	β-Ketoester	Amine	Product	Yield (%)
1	Benzaldehyde	Ethyl acetoacetate	Ammonia	1,4- Dihydropyridine 3a	89
2	4-Nitrobenzaldehyde	Methyl acetoacetate	Methylamine	1,4- Dihydropyridine 3b	85
3	Furfural	Dimethyl malonate	Ethylamine	1,4- Dihydropyridine 3c	82
4	Benzaldehyde	Ethyl acetoacetate	Ammonia	1,4- Dihydropyridine 3a	90
5	4-Chlorobenzaldehyde	Methyl acetoacetate	Methylamine	1,4- Dihydropyridine	88



IJFANS INTERNATIONAL JOURNAL OF FOOD AND NUTRITIONAL SCIENCES

ISSN PRINT 2319 1775 Online 2320 7876

Research Paper © 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, Iss 07, 2022

				3d	
6	4-Methoxybenzaldehyde	Dimethyl	Ethylamine	1,4-	84
		malonate		Dihydropyridine	
				3e	

Analysis:

• The desk illustrates the adaptability of the microwave-assisted 1,4-dihydropyridine synthesis catalysed with the aid of [BMIM][HSO4]. With a variety of aromatic and aliphatic aldehydes, β-ketoesters, and amines, the reaction is effective and produces the relevant products in precise to wonderful yields (eighty two-ninety%). This wide range of substrates indicates that several functional organizations, inclusive of methoxy (-OCH3), chloro (-Cl), and nitro (-NO2) groups, are tolerated via the reaction. This makes it viable to create a whole lot of 1,4-dihydropyridine derivatives, which could be used in remedies and biology. Significantly, under microwave irradiation, the reaction is effective and requires only short reaction intervals (three minutes) and slight temperatures (one hundred°C). As a result, the technique is quicker and uses less strength than traditional strategies. In addition, there are some blessings to the use of [BMIM][HSO4] as a catalyst, including its facile separation from the reaction mixture, adjustable acidity, and reusability. This enhances the process's universal sustainability and environmental friendliness.

The catalyst is recycled

With only a little reduction in interest, the [BMIM][HSO4] catalyst was efficiently recycled and utilised again for some reaction cycles. With a touch of water extraction, the catalyst can be readily extracted from the reaction aggregate and repurposed without requiring further purification. The most effective 1,4-dihydropyridine yield was over 85 percent after 5 cycles, indicating the excessive stability and reusability of the [BMIM][HSO4] catalyst.

Suggested method

Suggested Mechanism

The following critical degrees are concerned with the [BMIM][HSO4]-catalyzed 1,4-dihydropyridine synthesis, in keeping with the suggested mechanism:

- 1. β -ketoester activation: The [BMIM][HSO4] catalyst donates a proton to the β -ketoester carbonyl institution, functioning as an acidic Brønsted acid. As a result, the carbonyl carbon becomes more electrophilic and susceptible to nucleophilic attack.
- 2. Nucleophilic attack of the amine: An intermediate imine is fashioned when a free amine molecule hits the activated β -ketoester's electrophilic carbonyl atom.
- 3. Knoevenagel condensation procedure among the imine intermediate and the aldehyde consequences within the formation of a conjugated dihydropyridine intermediate.



- 4. Cyclization and product formation: The very last 1,4-dihydropyridine product is shaped by means of intramolecular cyclization of the conjugated dihydropyridine intermediate, which is aided by the acidic proton from the catalyst.
- 5. Catalyst regeneration: In the response cycle, the protonated catalyst is renewed, making it possible for it to participate in later cycles and boost the method's usual efficiency.

This process gives a tenable reason for the 1,4-dihydropyridine synthesis catalysed through [BMIM][HSO4] that has been demonstrated to be efficient and selective. It draws attention to how the catalyst helps activate the reactants and advance important response ranges. To improve the advised mechanism and gain additional knowledge of the response manner, extra studies are probably performed along with laptop modelling and kinetic studies.

Evaluation against traditional strategies

Compared to conventional strategies, the [BMIM][HSO4]-catalyzed microwave-assisted synthesis of 1,4-dihydropyridines has some blessings, such as:

- Faster response times: In comparison to traditional heating strategies, microwave irradiation substantially shortens the reaction time, normally most effective for three minutes rather than many hours. This substantially increases the synthesiser's productivity and performance.
- Greater yields: When [BMIM][HSO4] is used as a catalyst, yields are extra and frequently surpass 85% as compared to conventional catalysts, indicating enhanced manner performance and selectivity.
- Broader substrate scope: Compared to different present methods, the microwave-assisted approach substantially expands the spectrum of reachable 1,4-dihydropyridine derivatives by tolerating amines, β-ketoesters, and extraordinary aldehydes.
- Energy efficiency: Compared to traditional heating, microwave irradiation is an extrapower-efficient heating technology that minimises electricity intake and environmental impact.
- Reusability of the catalyst: There are both economic and environmental benefits to the [BMIM][HSO4] catalyst's clean restoration and reuse for many reaction cycles without pretty much dropping activity.
- Simplicity of use: Compared to a few conventional procedures, the microwave-assisted technique frequently requires less equipment and is less difficult to scale up.

Conclusion

In the microwave-assisted synthesis of one,four-dihydropyridines, this work demonstrates the high-quality effectiveness and flexibility of [BMIM][HSO4] as a catalyst, yielding first-rate consequences (as much as ninety%) in short times (3 mins) and at slight temperatures (a hundred°C). The catalyst has splendid stability and recyclability, proving its usefulness for several cycles without sacrificing activity. This allows for a vast variety of substrates to be used, as a result increasing the spectrum of 1,4-dihydropyridine derivatives that are to be had. Based on a cautioned Brønsted acid catalysis mechanism, this approach differs from present techniques in that it is more eco-friendly, efficient, and conserves power. Further studies are expected to



study extra giant uses in the synthesis of extra heterocyclic compounds, the utilisation of substitute catalysts, the examination of biological processes for possible therapeutic pathways, the optimisation of conditions for improved yields and wider tiers of substrates, and the development of mechanistic insights through sophisticated methodologies. There is an awesome deal of capacity in this technology for the efficient and sustainable synthesis of important chemical substances, which requires additional research and improvement.

Acknowledgement

The authors express sincere thanks to principal, SMBST College of Arts, Science and Commers Sangamner for providing necessary facilities. Also grateful to SSGM College Koparagon.

References

1. Baleizão, C., Gigante, B., Reis, M., & Martins, M. A. P. (2010). Ionic liquids as catalysts for the synthesis of 1,4-dihydropyridines: A review. Catalysis Communications, 12(1), 43-52.

2. Chhikara, B. S., & Sharma, N. (2019). [BMIM][HSO4]: A green and efficient catalyst for the synthesis of 1,4-dihydropyridines and their biological importance. Journal of Molecular Liquids, 273, 526-536.

3. El-Faham, A., El-Zahabi, H. S., El-Khateeb, M., & Awadallah, A. M. (2012). Microwave irradiation: A green and efficient technique for the synthesis of new 1,4-dihydropyridines using ionic liquid as catalyst. Journal of Heterocyclic Chemistry, 49(3), 600-608.

4. Firouzabadi, H., Iranpoor, N., & Hazarkhani, H. (2005). A convenient synthesis of 1,4dihydropyridines catalyzed by [BMIM]HSO4 under solvent-free conditions. Synlett, 2005(12), 2017-2020.

5. Khazaei, A., Zolfigol, M. A., & Moosavi-Zare, A. R. (2010). A facile synthesis of 1,4dihydropyridines under microwave irradiation using [BMIM][HSO4] as a reusable catalyst. Journal of the Iranian Chemical Society, 7(2), 327-332.

6. Li, C. J., & Song, G. (2001). Ionic liquids as green catalysts for the synthesis of 1,4dihydropyridines. Journal of Organic Chemistry, 66(24), 8199-8202.

7. Liu, Y., Li, S., Zheng, J., & Zhang, L. (2018). Efficient synthesis of 1,4-dihydropyridines using [BMIM][HSO4] as a recyclable catalyst under microwave irradiation. Chinese Journal of Catalysis, 39(2), 225-230.

8. Mhaske, S. B., & Pore, V. S. (2012). Ionic liquids as recyclable and efficient catalysts for the synthesis of 1,4-dihydropyridines under microwave irradiation. Catalysis Communications, 24, 63-67.



9. Mohammadi, A. A., Hasaninejad, A. R., & Shamsipur, M. (2014). One-pot four-component synthesis of 1,4-dihydropyridines catalyzed by [BMIM]HSO4 under microwave irradiation. Journal of the Iranian Chemical Society, 11(2), 323-331.

10. Salehi, P., Dabbagh, H. A., & Baghbanzadeh, M. (2012). An efficient and green synthesis of 1,4-dihydropyridines using [BMIM][HSO4] as a reusable catalyst under microwave irradiation. Tetrahedron Letters, 53(12), 1758-1761.

11. Varma, R. S. (2002). Solvent-free and microwave-assisted organic synthesis. Green Chemistry, 4(4), 102-110.

12. Yadav, J. S., Reddy, B. V. S., & Sunitha, G. (2013). A highly efficient and recyclable catalyst [BMIM][HSO4] for the synthesis of 1,4-dihydropyridines under microwave irradiation. Green Chemistry Letters and Reviews, 6(3), 231-236.

13. Zhang, J., Zhang, Z., Zhang, B., & Deng, Y. (2009). One-pot synthesis of 1,4dihydropyridines catalyzed by ionic liquid [BMIM][HSO4] under microwave irradiation. Helvetica Chimica Acta, 92(1), 175-181.

14. Zhou, Y., Yang, Y., Yang, T., & Zhang, T. (2011). A green and efficient synthesis of 1,4-dihydropyridines

