RSC Advances

REVIEW

View Article Online
View Journal | View Issue

Check for updates

Cite this: *RSC Adv.*, 2025, **15**, 40912

Recent trends in ionic liquid-mediated synthesis of thiazoles: toward greener methodologies

Shital Mohurle and Barnali Maiti *

Thiazole moieties represent a vital category of heterocycles, offering versatile uses across drug development, agricultural formulations, and advanced materials. Nevertheless, conventional methods for their synthesis frequently depend on toxic solvents and rigorous conditions, which raise significant environmental and safety concerns. Recently, ionic liquids (ILs) have gained recognition as sustainable and versatile solvents due to their exceptional physico-chemical characteristics, namely minimal vapor pressure, adjustable polarity, and recyclability. This review focuses on synthesizing thiazole derivatives through ionic liquid-mediated strategies, emphasizing their alignment with the principles of green chemistry. Recent advancements in catalyst-free protocols and recyclable ionic liquid (IL) systems are discussed in detail, along with comparisons to conventional methods in terms of green metrics. This review integrates recent advancements to deliver a focused and thorough summary of green synthetic approaches for thiazoles between 2004 and 2025. It highlights the current limitations and proposes directions for future research toward greener and more scalable methodologies.

Received 4th August 2025
Accepted 15th October 2025

DOI: 10.1039/d5ra05665a

rsc.li/rsc-advances

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

1. Introduction

Achieving eco-friendly synthetic routes presents a key challenge in the advancement of heterocyclic chemistry.[1] Green chemistry is a proactive scientific discipline focused on designing and synthesizing chemical compounds that exert minimal Influence on ecological systems. The swift advancement of sustainable chemistry reflects a growing awareness that eco-conscious methodologies deliver not only ecological benefits but also optimized efficiency, selectivity, and atom economy in addressing pressing industrial needs.[2,3] This progress is exemplified by advanced catalytic systems, including nanotechnology-based and atomically precise catalysts, which enable the selective, efficient, and sustainable synthesis of complex heterocycles. Together, these developments highlight

Department of Chemistry, School of Advanced Sciences, Vellore Institute of Technology, Vellore-632014, India. E-mail: barnalimaiti.m@gmail.com; barnali.m@vit.ac.in

Shital Mohurle

Shital Mohurle was born in Sirpur, Maharashtra, India, in 1997. She earned her B.Sc. degree in Chemistry from Dr Ambedkar College, Nagpur (DACN), Maharashtra, in 2018, followed by an M.Sc. in Chemistry from Vellore Institute of Technology (VIT), Vellore, in 2020. She is currently pursuing her PhD in Chemistry at VIT, Vellore, under the supervision of Dr Barnali Maiti. Her research interests include catalyst design, asymmetric synthesis, and ionic liquid-assisted organic synthesis.

Barnali Maiti

Barnali Maiti was born in West Bengal, India, in 1978. She earned her M.Sc. in chemistry from Vidyasagar University in 2003 and completed her PhD under Professor Chung-Ming Sun at National Chiao Tung University, Taiwan, in August 2011. Following her PhD, she spent 22 months as a post-doctoral fellow in the laboratory of Professor Hsing-Wen Sung at National Tsing Hua University, Taiwan. In 2015, she joined the Chemistry Department at Vellore Institute of Technology as an assistant professor and currently serves as an associate professor. Her research focuses on designing and synthesizing novel ionic liquid-supported bifunctional organocatalysts and exploring their applications in various organic reactions.

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM. This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

the convergence of green chemistry principles and synthetic performance, paving the way for greener industrial processes and novel therapeutic discoveries.[4] Heterocyclic chemistry is a cornerstone of research in organic chemistry, due to its broad applications and significance.[5] In modern and medicinal chemistry, heterocyclic compounds containing nitrogen and sulfur, such as thiazoles, have garnered considerable attention because of their favourable electronic behaviour and structural versatility, which support a wide spectrum of chemical and biological functionalities.[6] Thiazole, systematically known as 1,3-thiazole, belongs to the azole family of heterocycles and features a five-membered cyclic framework with three carbon atoms, along with a sulfur and a nitrogen atom located at positions 1 and 3, respectively.[7] The development of synthesizing compounds containing the thiazole moiety has been continuously progressing due to its importance in liquid crystals,[8] sensors,[9] dyes,[10] pigments,[11] and catalysts.[12] Thiazole derivatives occur naturally in numerous bioactive compounds across diverse biological sources and have profound applications in materials science, pharmaceutical chemistry, and agrochemicals, highlighting their significant importance across multiple industries.[13] There are over 20 FDA-approved drugs that contain a thiazole scaffold.[14] In addition, numerous thiazole-containing drugs are used clinically, such as Cefotaxime,[15] serves as an effective antibiotic for managing infections of the lower respiratory tract and the genitourinary system; simeprevir[16] serves as an antiviral agent specifically indicated for chronic HCV treatment; ritonavir[17] and cobicistat,[18] which act as antifungal drugs for the treatment of HIV/AIDS; sulfathiazole,[19] is an antimicrobial agent employed in the treatment of pyogenic skin infections; and nitazoxanide,[20] is an antiparasitic agent which is prescribed for managing diarrheal illnesses associated with *Cryptosporidium parvum* and *Giardia lamblia*.

Dasatinib[21] act as a Oncology drug, aimed at addressing chronic myelogenous leukemia, acotiamide[22] functions as a gastrointestinal drug for the treatment of functional dyspepsia, edoxaban[23,24] act as an angio-cardiopathic drug for the treatment of Stroke and systemic embolism, meloxicam[25] is classified as a musculoskeletal agent and is commonly used for managing moderate to severe pain and febuxostat[26,27] serves as a therapeutic option for treating hyperuricemia associated with gout. Moreover, alpelisib[28] is utilized for managing breast cancer, and lusutrombopag is another drug molecule used in oncology (Fig. 1). Owing to their broad spectrum of bioactivity, thiazole-based compounds are considered promising candidates for the development of treatments targeting numerous diseases.[29,30] Our research area focuses on the green synthesis of thiazole moieties using ionic liquids, in line with sustainable chemistry principles.[31] This review offers the first in-depth analysis of thiazole synthesis mediated by ionic liquids,

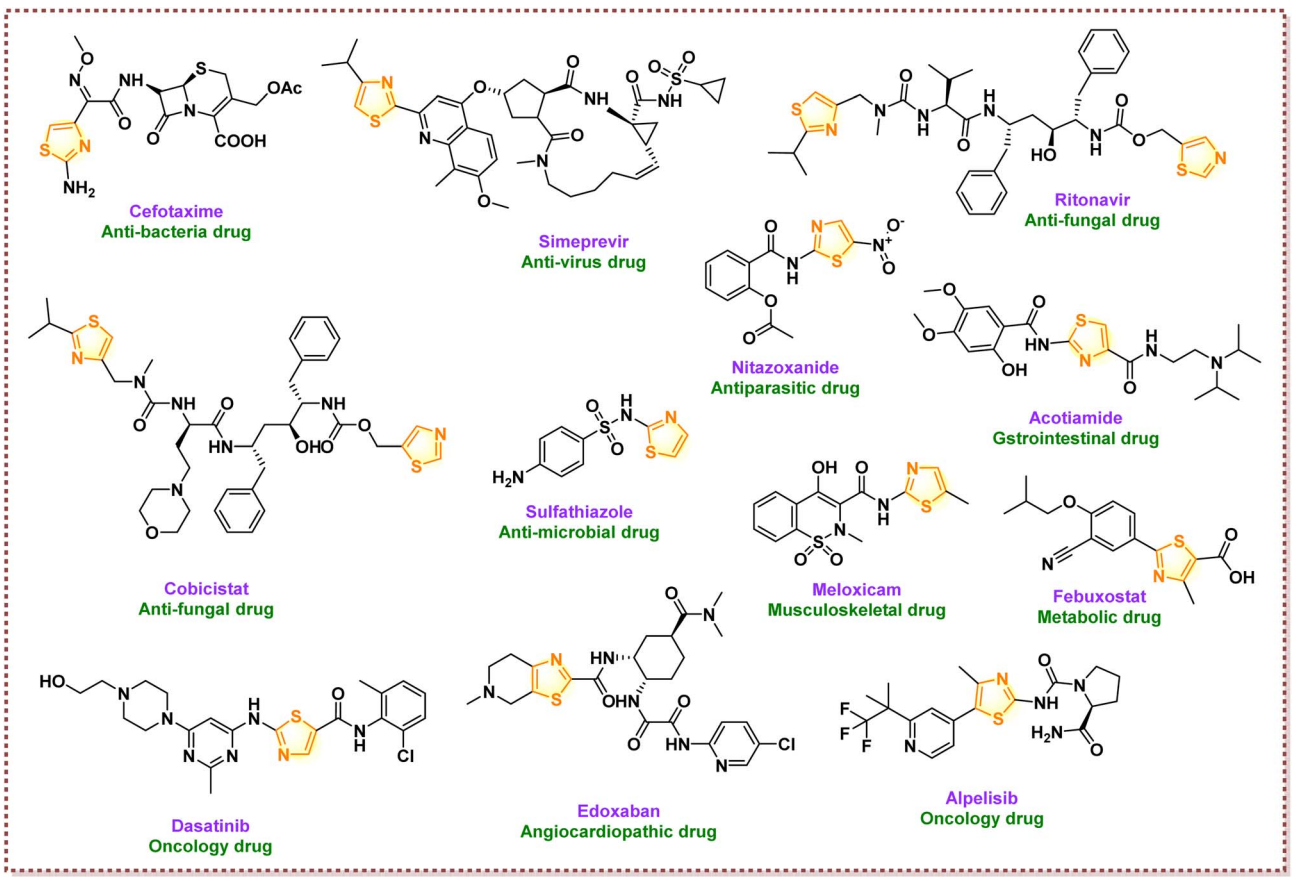


Fig. 1 FDA-approved therapeutic agent featuring a thiazole scaffold.

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM. This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

systematically categorized based on addressing the behaviour of the ionic liquid, possibly serving as a passive medium, a dual solvent-catalyst system, a supported or immobilized system, or in comparison with other non-ionic liquid green approaches. To the best of our knowledge, no previous review has comprehensively addressed this perspective, making our work a novel contribution. By highlighting the synthetic potential and environmental advantages of ionic liquids, this review aims to fill a critical gap in the literature and guide future innovations in green heterocyclic chemistry.

2. Thiazole moieties: chemistry and traditional synthetic strategies

Thiazole, systematically known as 1,3-thiazole, is an aromatic heterocyclic compound of notable chemical interest, possessing the molecular formula C_3H_3NS and a molecular weight of 85.128 g mol^{-1}.[32] Thiazole is a low-molecular-weight heterocyclic compound that exists as a volatile, flammable liquid with a characteristic pale-yellow appearance. It exhibits a boiling point in the range of 116–118 °C and possesses a dipole moment of 1.6 D.[33] Thiazole exhibits aromatic character similar to pyridine, consistent with Hückel's rule, wherein the sulfur atom contributes a lone pair of non-bonding electrons to the π-electron system (Fig. 2).[34]

Thiazole derivatives, owing to their planar and aromatic nature with enhanced electron delocalization compared to oxazole, serve as valuable model systems in chemical research.[35] The aromatic nature of the thiazole ring has been supported by ^{1}H NMR spectroscopy, with proton signals appearing in the range of 7.27–8.77 ppm, indicative of a pronounced diamagnetic ring current. Additionally, an infrared spectroscopic analysis (FTIR), performed within the 400–4000 cm^{-1} region, identified nine key vibrational modes.[36–38] Moreover, substitution at the C-2, C-4, and C-5 positions of the thiazole ring significantly influences its reactivity, potentially introducing ring strain and necessitating further structural evaluation.[39] For instance, the presence of a methyl group, an electron-donating substituent, at various positions on the thiazole ring enhances both its basicity and nucleophilicity. In contrast, introducing a strong electron-withdrawing group like a nitro moiety results in a noticeable decline in these electronic properties.[29,40] Thiazole derivatives have garnered considerable research interest owing to their broad range of applications. The key advantage lies in their accessible synthesis from readily available precursors through multiple methodologies, often affording high product yields.[41] Among the earliest and most notable methodologies are the Hantzsch synthesis, Cook–Heilbron synthesis, and Gabriel synthesis.[42]

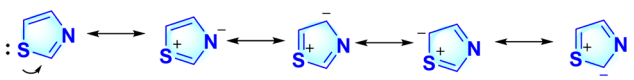


Fig. 2 Resonance forms of the thiazole compound.

2.1. Hantzsch synthesis

Among the various synthetic approaches, the Hantzsch thiazole synthesis was first reported in 1887 by the German chemist Arthur Hantzsch, which remains one of the most prominent methods for constructing the thiazole ring.[43] This is also known as synthesis from α-halocarbonyl compounds. This approach involves the condensation of α-haloketones **1** (or α-haloaldehydes) with thioamides or thioureas **2**, leading to the formation of substituted thiazoles **3**.[44] The α-carbon of the halo carbonyl is attacked by the thioamide sulfur atom nucleophilically, forming an intermediate that is then dehydrated to produce the corresponding thiazole. This method is valued for its simplicity, accessibility of starting materials, and ability to form thiazole rings under relatively mild conditions (Scheme 1).[45]

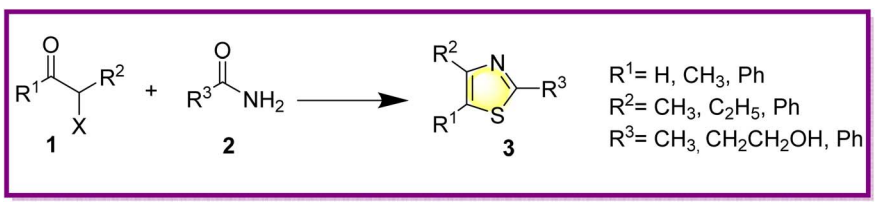
Furthermore, thiazolium salts **6** can be efficiently synthesized *via* a modified version of Hantzsch's thiazole protocol. This approach is particularly advantageous for preparing derivatives bearing aryl or heteroaryl substituents on the ring nitrogen, which are often inaccessible through direct alkylation. For instance, *N*-monosubstituted thioamides **5** have been successfully cyclized with α-halocarbonyl compounds **4**, affording thiazolium salts in excellent yields (Scheme 2).[46–48]

2.2. Cook–Heilbron synthesis

The Cook–Heilbron method, introduced by Allan Cook and Ian Heilbron in 1923, is also recognized as a method for synthesizing thiazoles.[49] The synthetic route involves combining α-aminonitriles **7** with dithioacids compounds, isothiocyanates **8**, and CS_2 to afford 5-aminothiazoles **9** under environmentally benign conditions.[50,51] This method is historically significant and was among the first to explore diverse thiazole-based precursors (Scheme 3).[52]

2.3. Gabriel synthesis

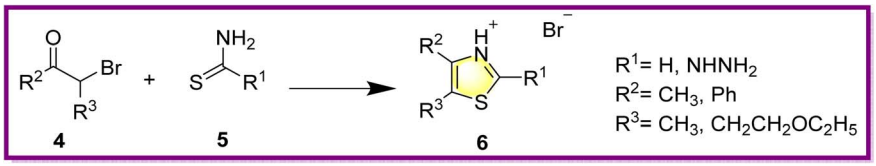
The Gabriel synthesis, also referred to as the Gabriel phthalimide method, was first introduced by the German chemist



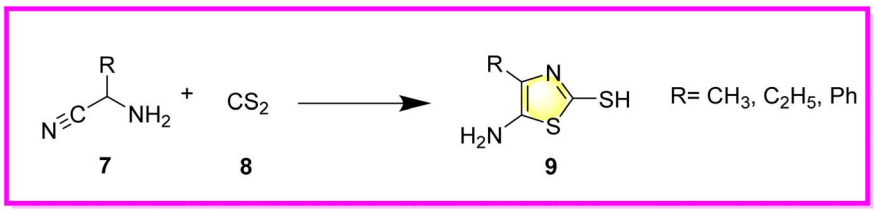
Scheme 1 Hantzsch synthesis of thiazole from α-haloketones and thioamides.

© 2025 The Author(s). Published by the Royal Society of Chemistry

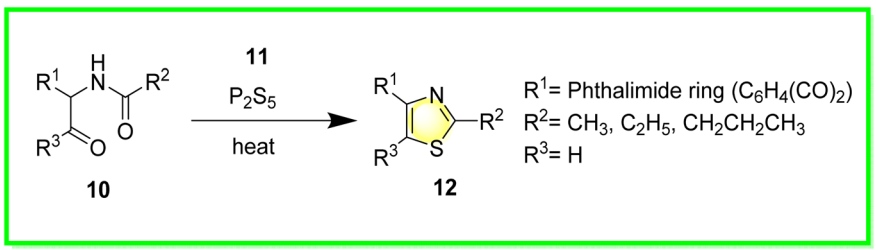
Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Scheme 2 Synthesis of thiazolium salts.



Scheme 3 Synthesis of thiazole from α-aminonitriles and carbon disulfide.



Scheme 4 Synthesis of thiazole from the condensation of acyl amino carbonyl compounds.

Siegmund Gabriel in 1888.[53] In the context of thiazole chemistry, this reaction represents a ring-closure transformation involving an acylamino-ketone **10** and phosphorus pentasulfide **11**, leading to the formation of 2,5-disubstituted thiazole derivatives **12**.[45] Mechanistically, this process is analogous to the synthesis of other five-membered heterocycles containing oxygen or sulfur, typically derived from 1,4-dicarbonyl precursors (Scheme 4).[54]

Collectively, these classical methods laid the foundation for thiazole synthesis, providing versatile access to core scaffolds that continue to inform modern synthetic strategies. Despite their historical importance and synthetic utility, traditional methods are commonly linked to harsh conditions, inefficient atom usage, and the employment of toxic or hazardous chemicals. As the field of synthetic chemistry continues to evolve toward more sustainable and innovative practices, the integration of green solvents and alternative reaction media has gained substantial momentum.[55] Within this context, ionic liquids have surfaced as a promising and transformative category of solvents, exhibiting unique chemical and physical traits that support environmentally sustainable practices.[56] The following section highlights the increasing significance of ionic liquids in current organic synthesis, emphasizing their application in green approaches to thiazole synthesis.

3. Ionic liquid (IL) in organic synthesis

3.1. Introduction to ionic liquids

Over the past few decades, the rise of green chemistry has spurred extensive research into designing compounds that offer improved environmental and health profiles.[56] Considering these factors, advancements in industrial and scientific research have significantly accelerated the development and large-scale production of ionic liquids.[57] Ionic liquids are a class of salts made up solely of ions, usually consisting of an organic cation combined with either an inorganic or organic anion, and are characterized by low melting points, often at or below 100 °C.[58,59] The extensive range of possible combinations between known cations and anions, estimated between 10^6 and 10^{18},[59] results in a broad range of ionic liquids, characterized by distinct properties like resistance to high temperatures, expansive electrochemical windows, and very low evaporation tendencies. These appealing attributes have garnered significant attention from both scientific researchers and industrial sectors (Fig. 3).[60]

3.2. Roles of ionic liquids in organic transformation

Ionic liquids (ILs) have been employed in green chemistry primarily because they are non-flammable, recyclable, and non-

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

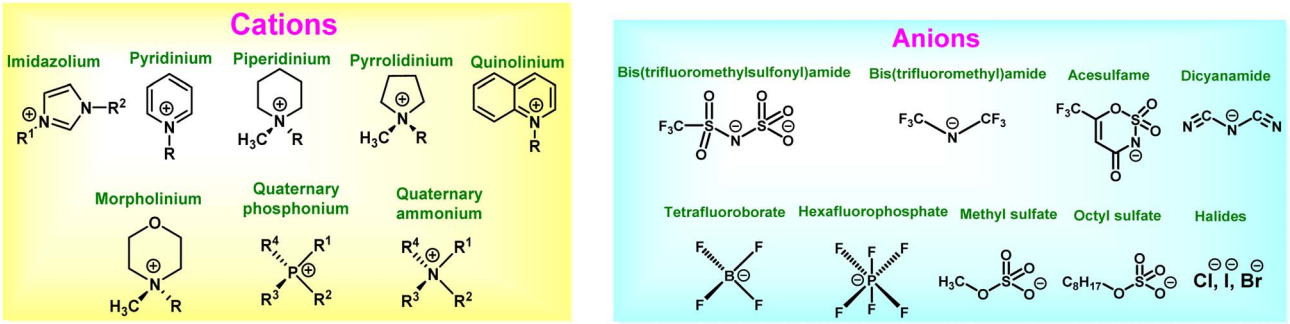


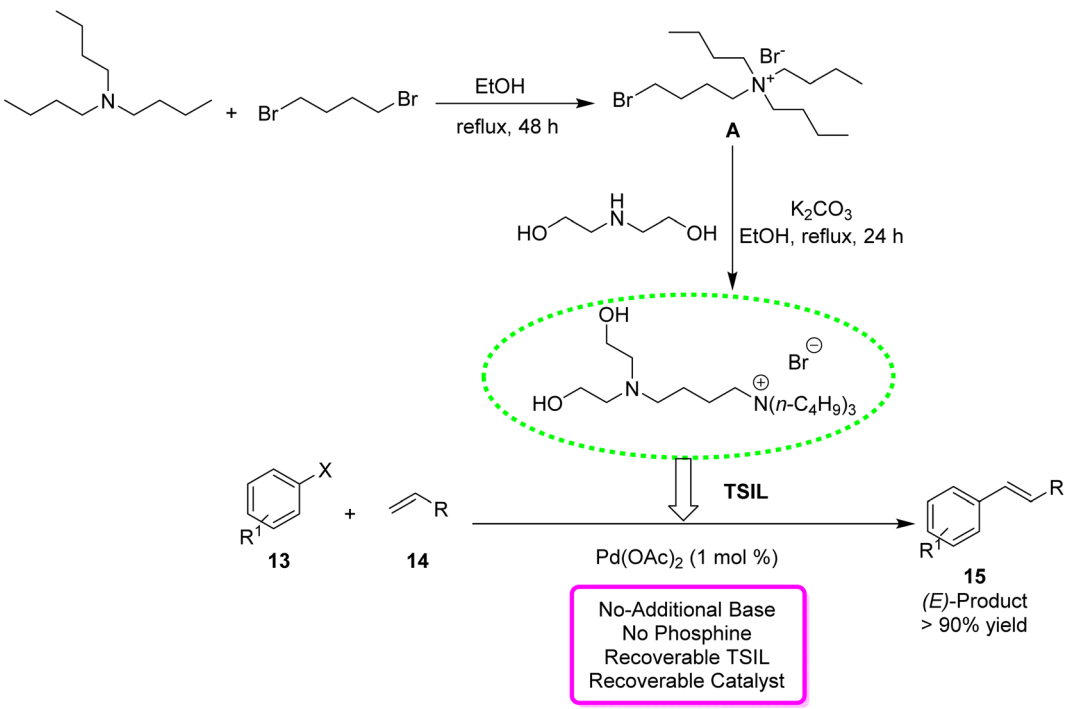
Fig. 3 Varied structural features of ionic liquid constituents.

volatile, which lowers the risks of human exposure and environmental pollution.[59] Furthermore, task-specific ionic liquids (TSILs), which are designed for increased reactivity or selectivity in particular reactions, are produced by the capacity to fine-tune their structures.[61] These features contributed ILs queued up with important green chemistry principles, including waste reduction, energy efficiency, and cleaner solvents.[57] ILs play multiple roles in organic synthesis, serving as solvents, co-solvents, and occasionally as catalysts. They have been successfully used in esterification, aldol condensations, oxidations, reductions, multicomponent reactions, and cross-coupling reactions.[62,63] Their ionic environment often stabilizes reactive intermediates and improves selectivity. For instance, task-specific ILs function as a solvent, base, and ligand in unison, as well as a reaction medium for the palladium-catalysed Heck reactions under phosphine-free conditions, yielding good to excellent results (Scheme 5).[63]

3.3. Advantages over traditional solvents

Ionic liquids present several benefits when compared with conventional volatile organic solvents:

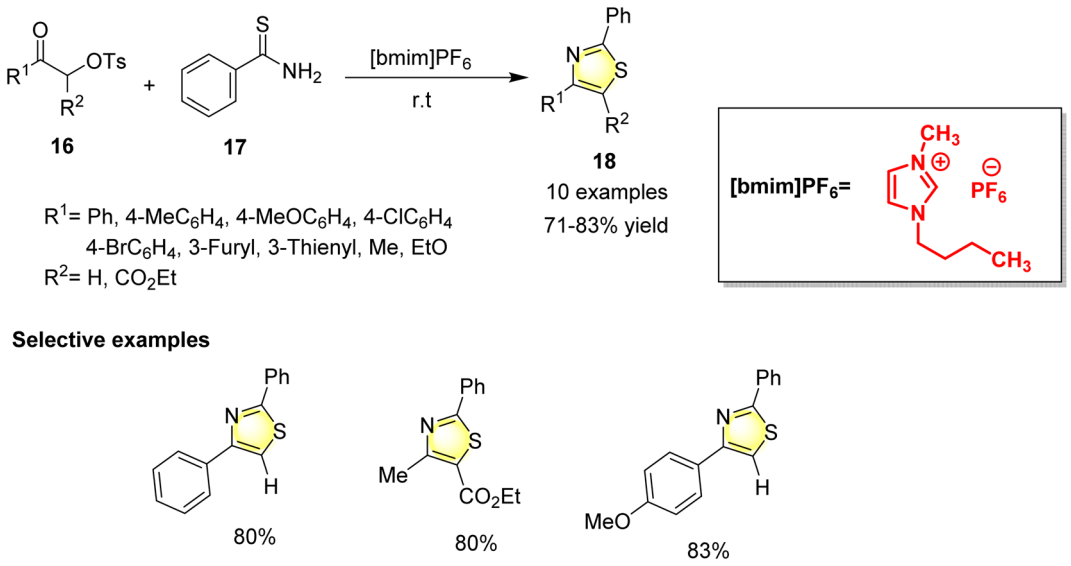
- Non-volatility: this significantly reduces the need for solvent recovery systems and minimizes the environmental emissions associated with their use.[64]
- High thermal and chemical stability: ionic liquids exhibit superior thermal and chemical stability compared to conventional organic solvents, allowing their effective use under demanding conditions such as elevated temperatures and reactive environments.[65]
- Recyclability and reusability: ILs can often be reused without significant loss in performance.[64]
- Tunability: through modification of their cation–anion composition, ionic liquids can be tailored for specific applications, giving rise to task-specific ionic liquids (TSILs) with improved efficiency and selectivity in chemical reactions.[66]



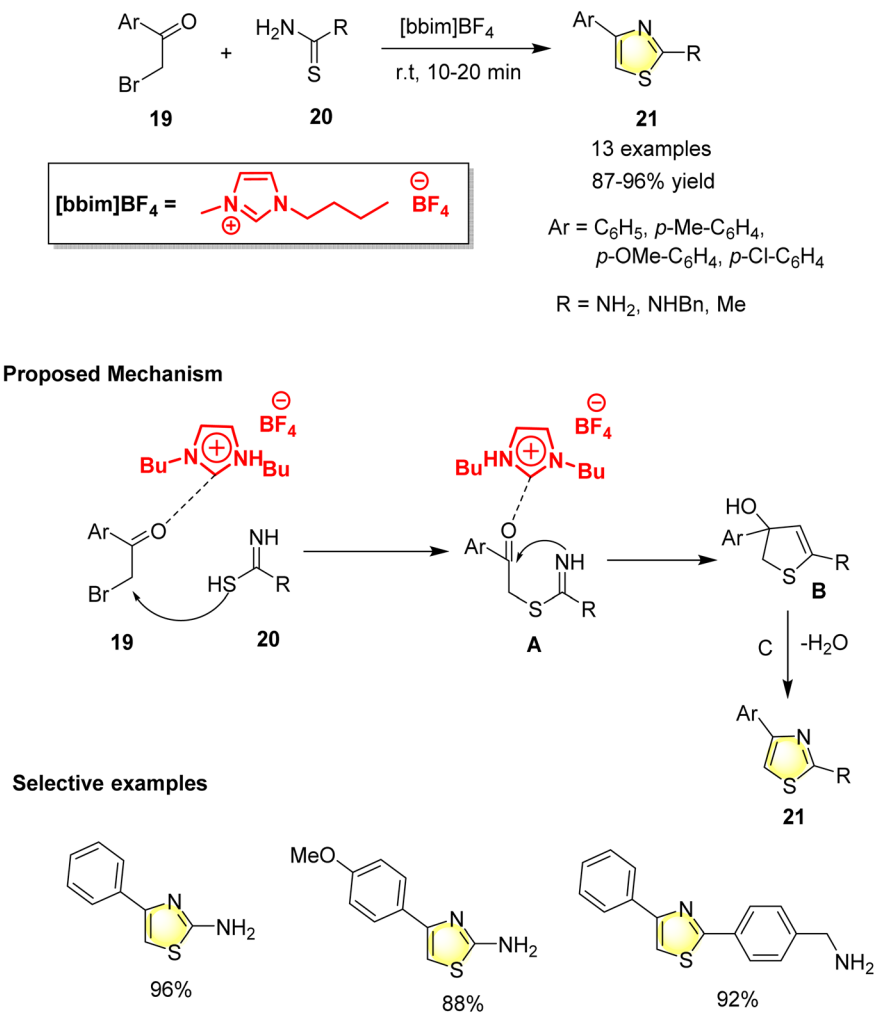
Scheme 5 Preparation of a functionalized ionic liquid for use in the Heck reaction.

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

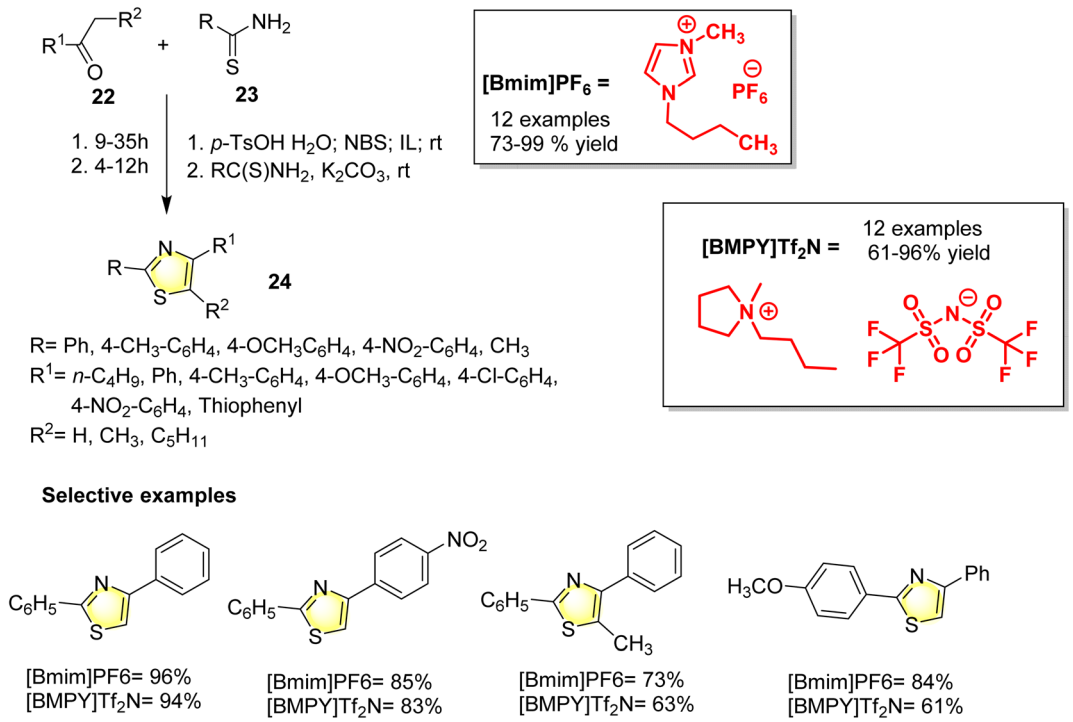


Scheme 6 Synthesis of thiazole using the ionic liquid [bmim]PF_6.



Scheme 7 Synthesis of thiazole using ionic liquid [bbim]BF_4.

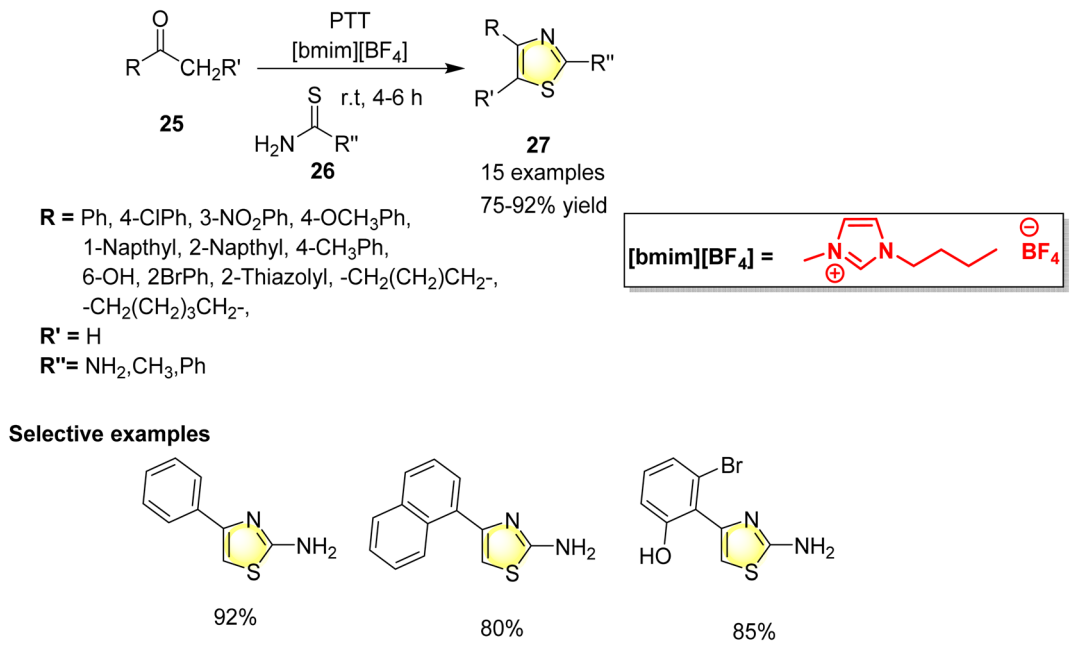
Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Scheme 8 Preparation of thiazole in [bmim]PF_6 and [bmpy]Tf_2N based ionic liquid.

• Reduced toxicity and environmental impact: although the toxicity profiles of certain ionic liquids remain under investigation, many are considered environmentally friendlier substitutes for traditional solvents. The emergence of sustainable ILs, like those based on choline and deep eutectic solvents, reflects a growing commitment to minimizing the ecological impact of chemical processes.[67,68]

• Green catalysis and reaction efficiency: in catalysis, ILs have demonstrated the ability to enhance reaction rates and selectivity, particularly in catalytic processes such as palladium-mediated coupling strategies and C–H bond functionalization reactions.[69] The ionic environment helps stabilize the catalyst and intermediates, leading to higher yields and faster reactions compared to traditional solvents. Additionally, ionic liquids can



Scheme 9 Synthesis of thiazole using ionic liquid [bmim]BF_4.

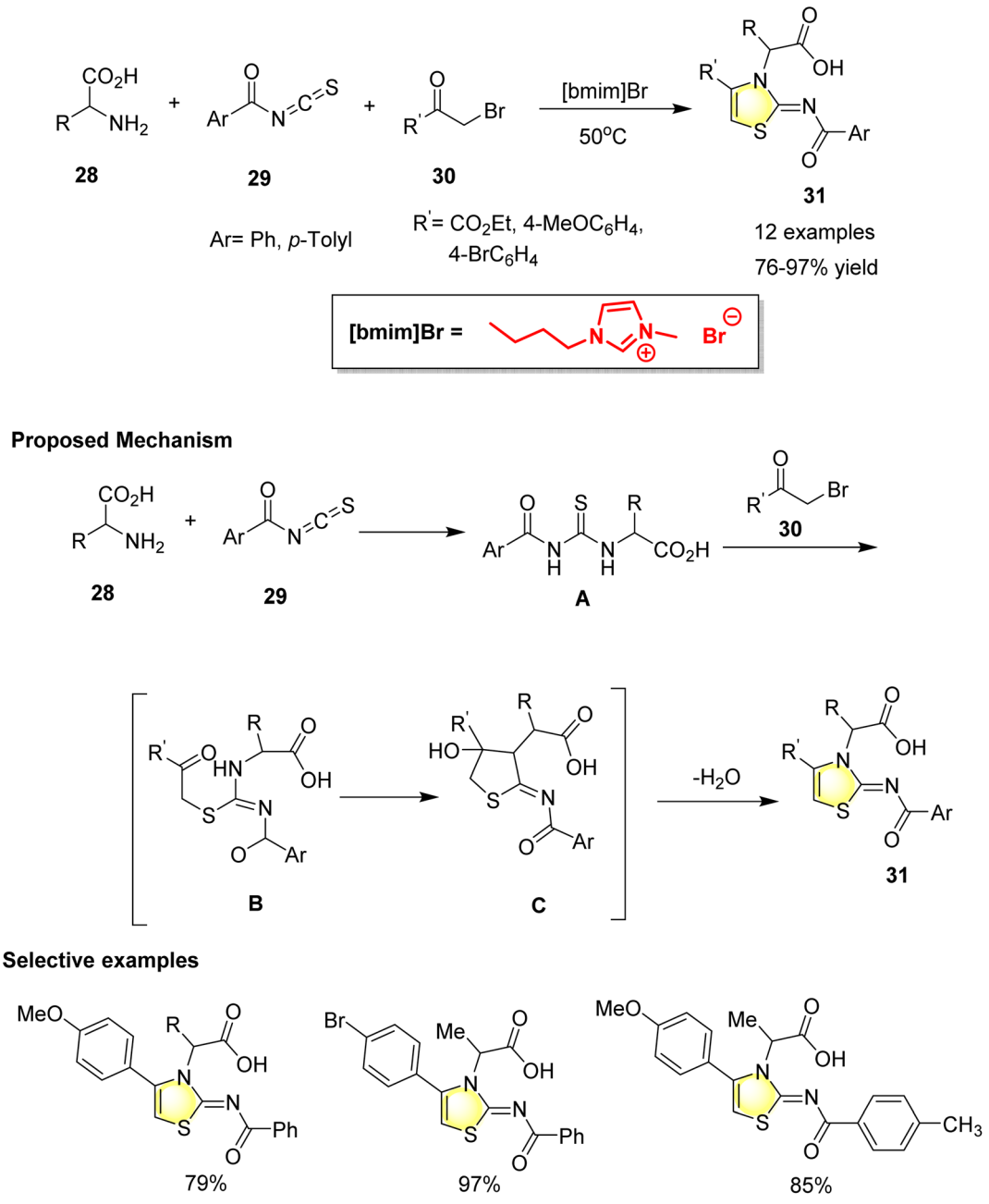
© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

simultaneously function as solvents and catalysts, making them highly effective for conducting one-pot synthetic processes.

During the last several years, the utilization of ionic liquids (ILs) has been expanded beyond general organic transformations and into the realm of heterocyclic synthesis, where their unique solvation and catalytic properties are being increasingly exploited. ILs are proving to be a valuable tool in enhancing reaction efficiency, improving yields, and reducing reaction times, all while promoting eco-friendly processes.[64,65] Thiazole-derived heterocycles are widely studied for their versatile therapeutic applications, including their ability to combat infections, alleviate inflammatory responses, and interfere with cancer cell proliferation.[70] The growing application of ILs in constructing thiazole frameworks stems from their efficiency in stabilizing transient species and enabling sustainable, atom-conserving synthetic routes.[71]

These advances underscore the integration of green chemistry principles with modern heterocyclic synthesis. In the following section, we delve into recent developments in thiazole synthesis mediated by ionic liquids, highlighting key strategies, reaction conditions, and the green benefits imparted by this innovative solvent system.



Scheme 10 Synthesis of thiazole using ionic liquid [bmim]Br.

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM. This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

4. Thiazole synthesis *via* ionic liquids: classification based on IL function

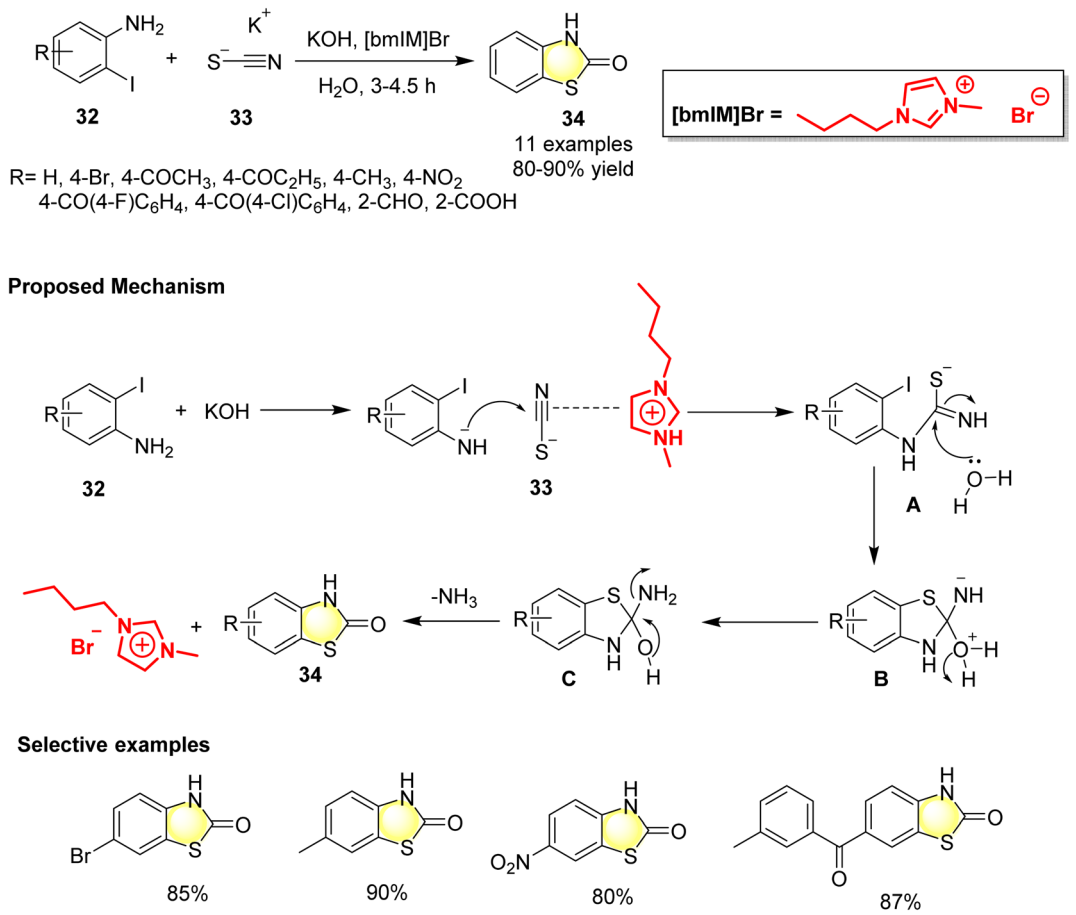
The synthesis of thiazole derivatives using ionic liquids (ILs) can be systematically categorized based on the functional role of the IL in the reaction medium, ranging from passive green solvents to task-specific catalysts and supported IL systems. This classification offers a clearer understanding of the mechanistic contributions and green potential of ionic liquids (ILs) in thiazole synthesis.

4.1. Ionic liquids as passive green solvents

In 2006, Hou *et al.*[72] introduced 1-butyl-3-methylimidazolium hexafluorophosphate [bmim]PF_6 as a green and recyclable reaction medium, presenting it as an eco-friendly substitute for traditional organic solvents in the synthesis of 2-phenylthiazoles **18**. This transformation involved the cyclocondensation of diverse α-tosyloxy-substituted ketones **16** in conjunction with aromatic thioamide **17**, carried out efficiently at ambient temperature in [bmim]PF_6, yielding good results (71–83%) of the desired product (Scheme 6). The key limitation of this methodology is the absence of detailed mechanistic elucidation, including the specific contributions of the cation and anion in stabilizing intermediates, which constrains a comprehensive understanding of the reaction pathway. Furthermore, the separation of products from ionic liquids is generally uncomplicated, with the added benefit that these solvents can be efficiently recovered and reused.

In the year 2007, Potewar *et al.*[73] outlined a resource-efficient and environmentally benign process for synthesizing 2,4-disubstituted thiazoles **21** by reacting phenacyl bromide **19** with substituted thiourea **20** in 1-butyl-3-methylimidazolium tetrafluoroborate [bbim]BF_4, an ionic liquid, under ambient conditions. The current approach enabled the instantaneous development of amino- and methyl-substituted 4-arylthiazole scaffolds, delivering high yields (87–96%) within 10–20 minutes. Moreover, it proved effective for the practical preparation of the anti-inflammatory agent fanetizole.

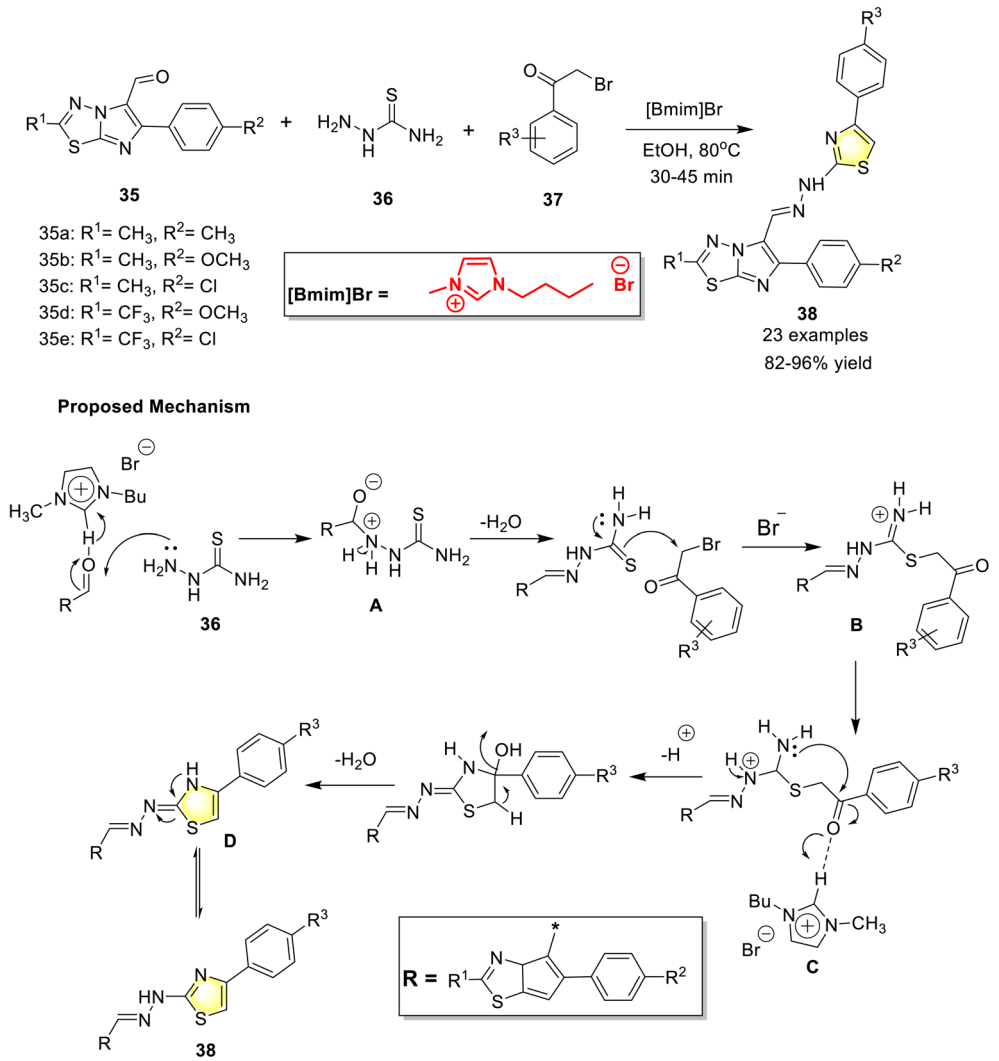
The reaction proceeds *via* the condensation step **A** of phenacyl bromide **19** with substituted thiourea **20** in the presence of an imidazolium-based ionic liquid (Scheme 7). The ionic liquid, through its Lewis or Brønsted acidic character, activates the carbonyl group of the phenacyl bromide by interacting with its oxygen, thereby increasing the electrophilicity of the carbon centre. The sulfur atom of the substituted thiourea **20** then attacks the activated carbonyl carbon, leading to the formation of an intermediate that undergoes an intramolecular cyclization



Scheme 11 Thiazole formation facilitated by [bmIm]Br ionic liquid.

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



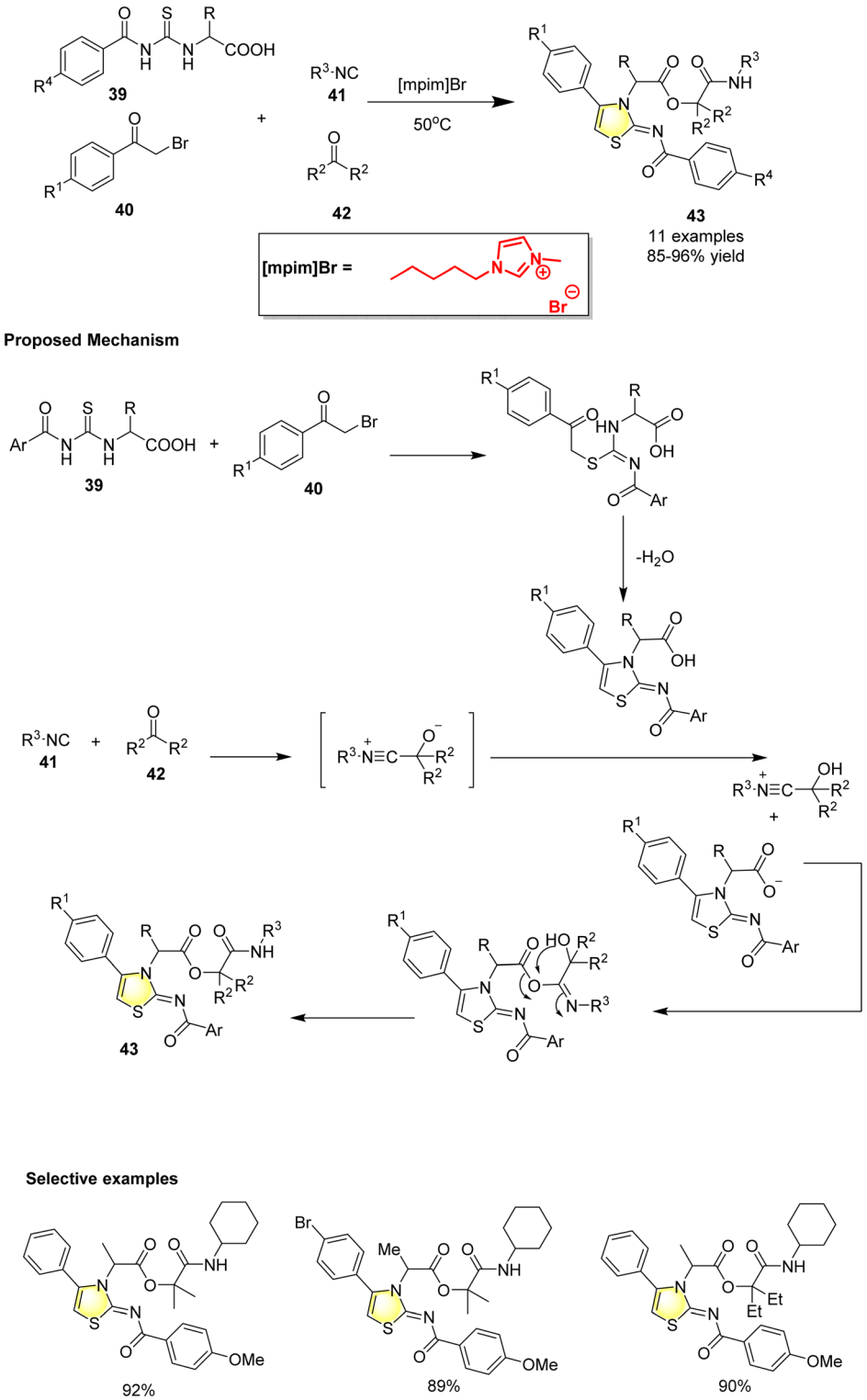
Scheme 12 Synthesis of thiazole using ionic liquid [Bmim]Br.

step **B** to yield a five-membered heterocyclic intermediate. Subsequent dehydration affords the corresponding thiazole derivative **21**. The methodology exhibits good functional group tolerance, proceeding smoothly with both electron-donating and electron-withdrawing substituents on the phenacyl bromide. The main advantages of the procedure include enhanced reaction efficiency, gentle processing parameters, superior output levels, and sustainability-oriented benefits, such as the exclusion of hazardous solvents and harmful catalytic agents, minimized by-product formation, and the potential for recycling and reusing the alternative reaction medium.

In 2011, Yuhta Izumisawa and co-authors[74] developed a clean and effective technique for synthesizing thiazoles **24** starting from ketones **22** and thioamides **23** using *N*-bromosuccinimide (NBS) within room-temperature ionic liquids (ILs). Notably, [bmim]PF_6 and [bmpy]Tf_2N were employed as recyclable media, enabling effective α-bromination of ketones involving *p*-toluenesulfonic acid as a catalyst, subsequently enabling a one-pot synthesis of thiazole derivatives upon the incorporation of thioamides (Scheme 8). These ILs demonstrated excellent reusability over several cycles without notable degradation in product yield or quality. The study underscores the utility of ILs as both solvents and catalytic systems for heterocyclic construction, particularly thiazole scaffolds with pharmaceutical significance. Moreover, the method exemplifies green chemistry principles by offering a sustainable and eco-conscious alternative to traditional organic solvent systems.

In the year 2012, Manoj Kumar Muthyala and co-workers[75] presented a green and efficient synthetic route to obtain 2,4-disubstituted thiazoles **27**. This process involved the reaction of substituted ketones **25** with phenyl trimethyl ammonium tribromide (PTT), functioning as a bromine source generated within the reaction medium, which is subsequently reacted with thioamide or thiourea **26**, all facilitated by the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate [bmim]BF_4 (Scheme 9). This methodology offers notable benefits such as the avoidance of irritant compounds, minimizing the reliance

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Scheme 13 Synthesis of thiazole using ionic liquid [mpim]Br.

on dangerous solvents while obtaining the products in yields of 75% to 92%.

Subsequently, in 2014, Ashraf S. Shahvelayati and co-authors[76] devised an effective multicomponent, one-pot procedure for synthesizing functionalized thiazol-2(3*H*)-imines **31** by combining α-amino acids **28**, aroylisothiocyanate **29**, and bromo-functionalized ketones at the alpha position **30** in an ionic liquid medium. The process was carried out using 1-butyl-3-methylimidazolium bromide[bmim]Br as the reaction medium at 50 °C, affording a variety of thiazole derivatives,

© 2025 The Author(s). Published by the Royal Society of Chemistry

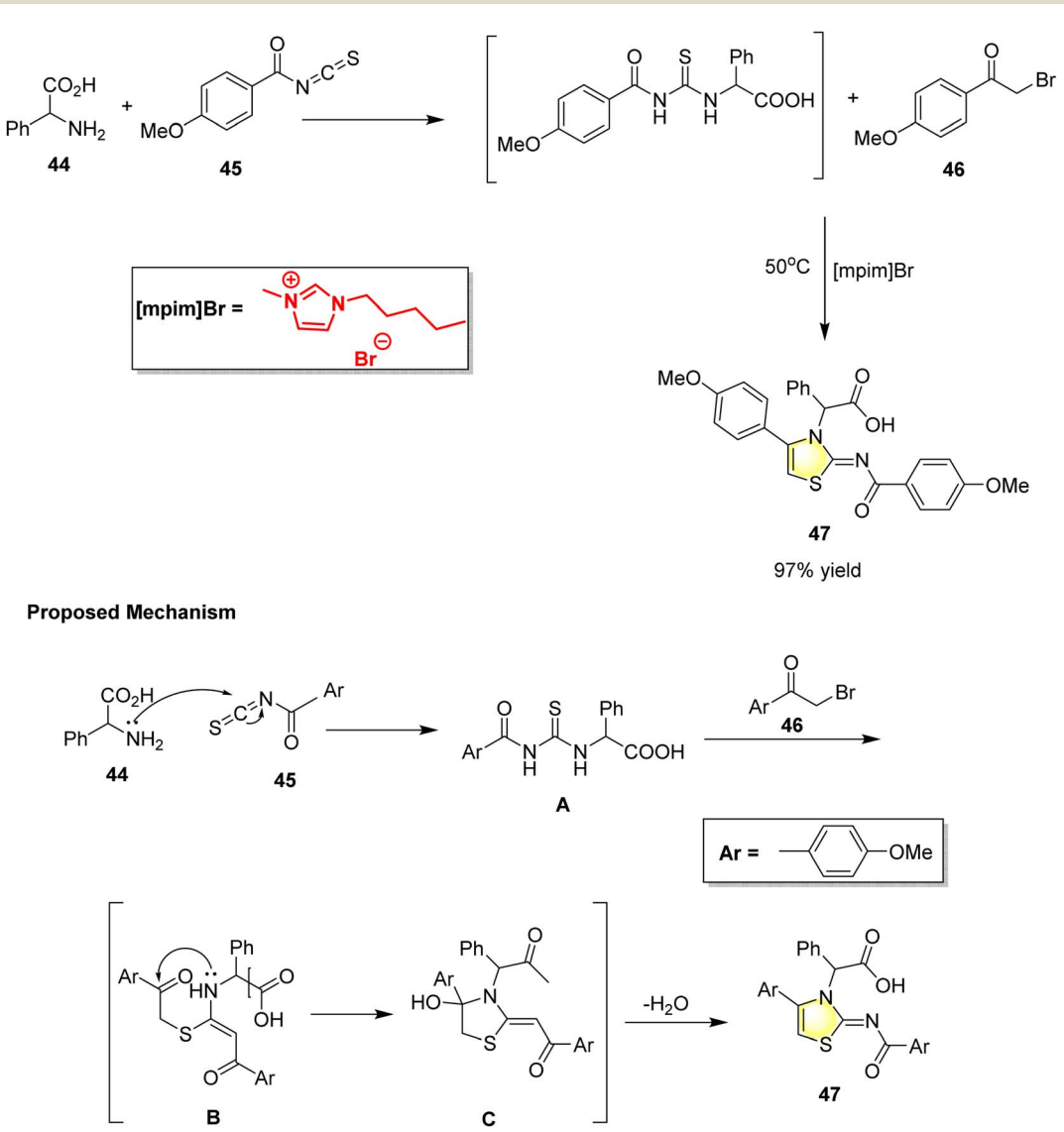
Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

affording excellent yields in the range of 76–97%. This approach underscores the effectiveness of ionic liquids as eco-friendly and reusable reaction media, providing improved selectivity and multiple reuses, all while maintaining chiral integrity, as demonstrated by optical rotation analysis of selected compounds (Scheme 10). The study demonstrates a practical and sustainable approach to constructing thiazole frameworks, contributing to the field of green heterocyclic synthesis.

While the precise mechanism of the reaction remains unclear, a reasonable pathway can be proposed to explain the formation of the final product.[73] Initially, the reaction proceeds through the formation of a thiourea derivative **A** *via* the condensation of α-amino acid **28** with aroylisothiocyanate **29**. The resulting intermediate then undergoes alkylation with a bromo-functionalized ketone **30** at the α-position in an ionic liquid medium, producing intermediate **B**. This intermediate subsequently undergoes intramolecular cyclization to generate intermediate **C**, which upon dehydration yields the desired functionalized thiazol-2(3*H*)-imines **31**.

Waseem and co-workers[77] developed an improved domino reaction technique for generating a series of biologically active benzothiazole-2(3*H*)-one derivatives **34a–k** under environmentally benign conditions. The method employed readily accessible 2-iodoanilines **32** and potassium thiocyanate **33** under the influence of the ionic liquid, 1-butyl-3-methylimidazolium bromide [bmIm]Br. The desired product was achieved in excellent yields up to 90% (Scheme 11). The various molar ratios of [bmim]Br and KOH were evaluated, and it was observed that a 15 mol% catalyst provided the maximum product yield. Interestingly, a further increase in the concentration of [bmim]Br led to a decline in yield, which is advantageous from an economic perspective due to reduced catalyst usage.

Furthermore, the reaction mechanism likely involves an initial nucleophilic attack by the sulfur anion of potassium thiocyanate **33** on 2-iodoaniline **32**. Subsequent deprotonation

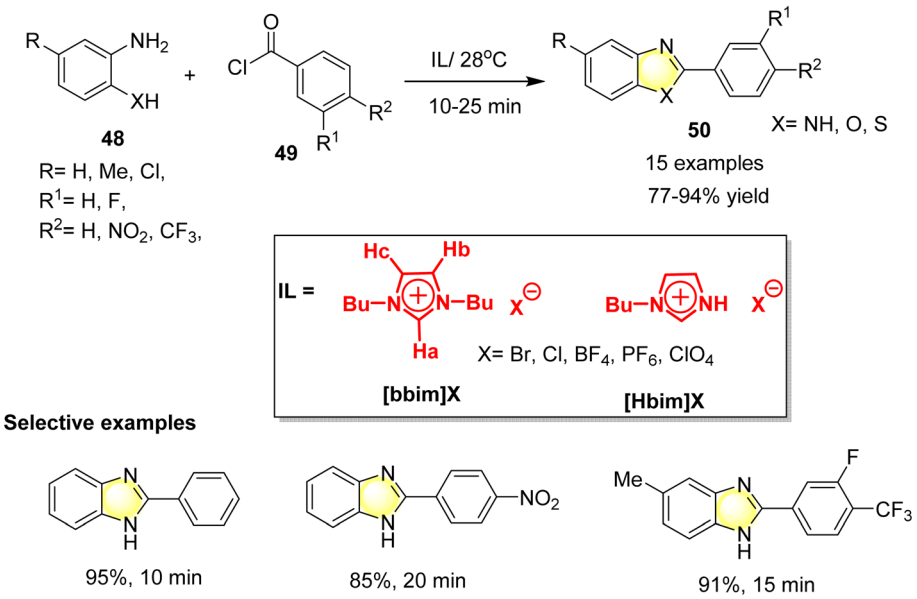


Scheme 14 Synthesis of thiazole using ionic liquid [mpim]Br.

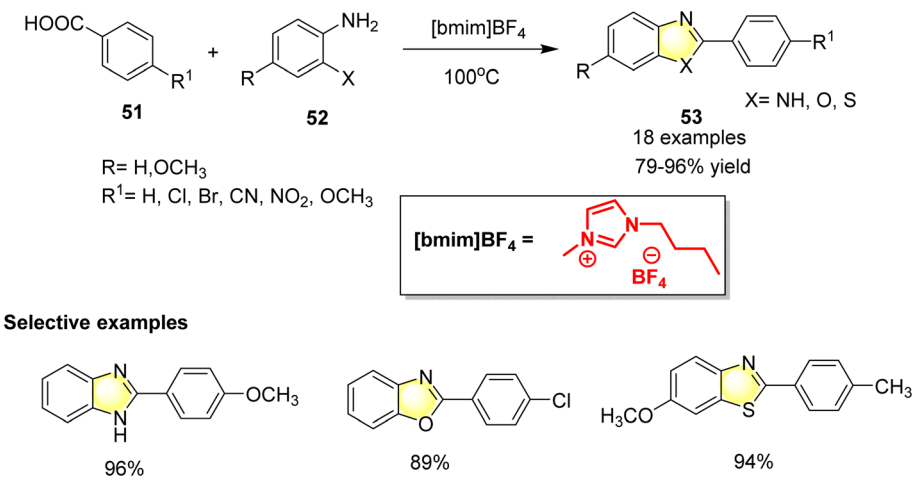
Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM. This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

of the $-NH_2$ group by the base generates an aniline nucleophile, which then attacks the electrophilic centre formed through the electrostatic interaction between the ionic liquid and the cyanate moiety of potassium thiocyanate, affording intermediate **A**. The activated sulfur species subsequently promotes the iodine displacement from 2-iodoaniline, resulting in intermediate **B**. This intermediate undergoes intramolecular cyclization to form intermediate **C**, which finally transforms into a stable and biologically active benzothiazole-2(3*H*)-one derivative **34**. The regeneration and subsequent application of [bmIm]Br following the completion of the reaction highlighted an excellent conclusion to the strategies. The reaction condition would also be beneficial for other heterocyclic syntheses. This technique stands out for its novelty and superior efficiency, offering shorter workup, higher yields, and reduced reaction times compared to existing methods.

In 2016, Ramprasad and co-workers[78] introduced a straightforward and effective single-step, three-reactant protocol for synthesizing thiazole derivatives **38**, utilizing the ionic liquid 1-butyl-3-methylimidazolium bromide [bmim]Br as the reaction medium. This methodology was carried out in a one-pot manner by combining fused heterocyclic aldehyde **35**, hydrazine-derived nucleophile **36**, and fluorinated phenacyl halide **37** in ethanol at 80 °C (Scheme 12). Moreover, the process was accomplished within a relatively limited duration of 30 minutes under the described conditions. The reaction proceeds through the condensation of a carbonyl compound with hydrazine-derived nucleophile **36** in the presence of [bmim]Br (ionic liquid), which activates the carbonyl group through hydrogen bonding, enhancing its electrophilicity. The resulting thiosemicarbazone intermediate **A** undergoes *S*-alkylation with phenacyl halide **37**, followed by intramolecular cyclization **B** *via*



Scheme 15 Synthesis of thiazole using both ionic liquids, $[Hbim]BF_4$ and $[bbim]BF_4$.

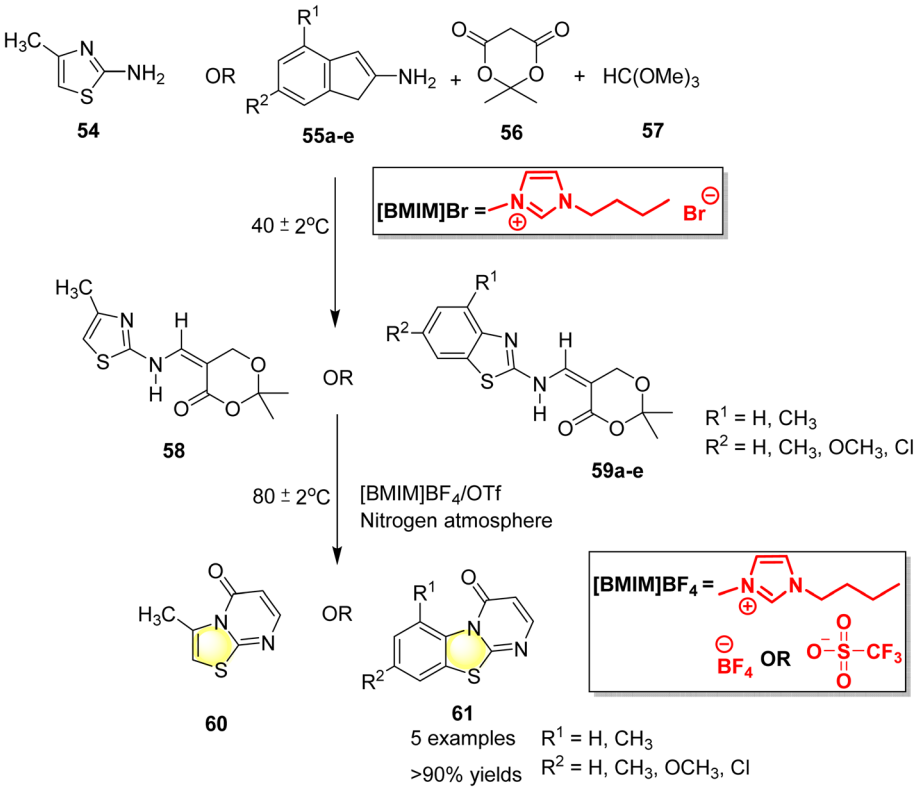


Scheme 16 Synthesis of thiazole using ionic liquid $[bmim]BF_4$.

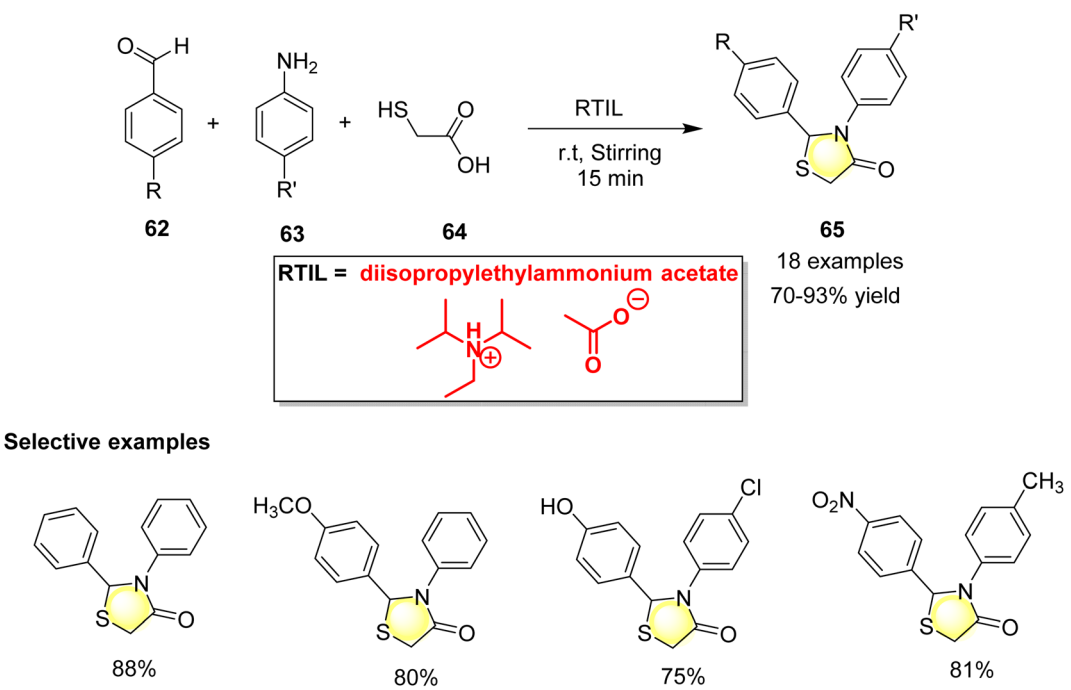
© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

nucleophilic attack of the azomethine nitrogen to form a thiazoline intermediate **C**. Subsequent dehydration and rearrangement afford the final thiazole derivative **38**, with the ionic liquid facilitating the process by stabilizing intermediates **D** and promoting efficient conversion under mild, solvent-free conditions. These derivatives **38** were isolated with high yields up to



Scheme 17 Eco-friendly synthesis of thiazole in [BMIM]Br/OTf medium.



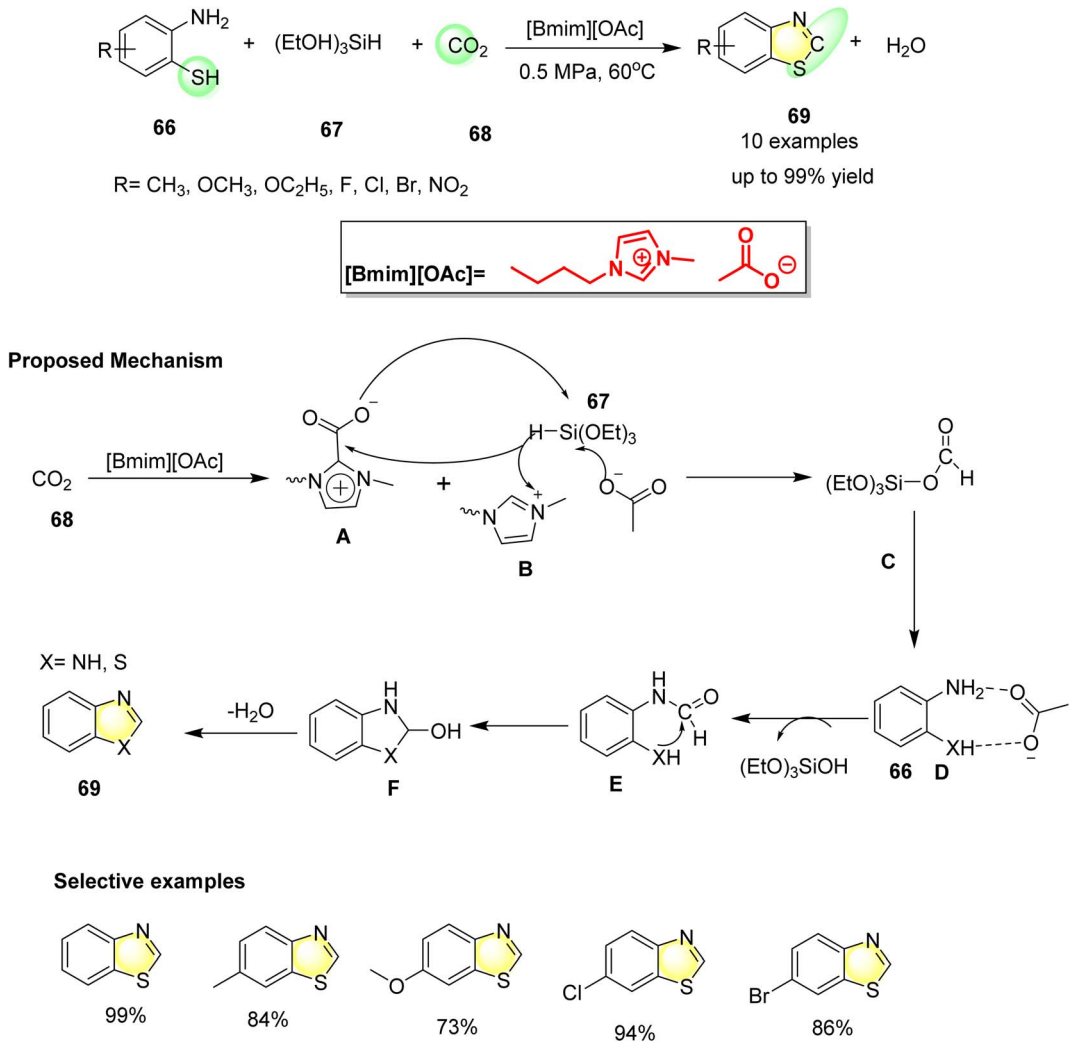
Scheme 18 Thiazole formation mediated by the ionic liquid DIPEAc.

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM. This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

82–96%. The compounds **38a–w** underwent *in vitro* analysis to assess their antitubercular activity against the *Mycobacterium tuberculosis* H37Rv strain. Among them, compound **38s** exhibited the most potent activity (MIC = 6.03 μM), surpassing standard drugs such as ethambutol and ciprofloxacin. These findings underscore the potential of IL-mediated synthesis and rational hybrid design in developing selective, potent antitubercular agents.

In the same year, Shahvelayati and co-authors[79] developed an efficient four-component reaction, performed in a one-pot manner without the need for the formation of functionalized thiazolodepsipeptide **43**, employing 1-methyl-3-pentylimidazolium bromide [mpim]Br as an eco-friendly ionic liquid medium. The reaction involves thiourea carboxylic acids **39**, phenacyl bromides **40**, isocyanides **41**, and ketones **42** under mild conditions (50 °C), yielding diverse thiazole–depsipeptide hybrids in good yields (up to 96%). Interestingly, the IL was effectively recovered and reused, as well as facilitated condensation and cyclization *via* the Passerini-tandem process. Based on the spectroscopic data obtained, the plausible reaction mechanism is illustrated in Scheme 13. The reaction begins with the *S*-alkylation of thiourea carboxylic acids **39** by phenacyl bromides **40**, which subsequently promotes cyclization, leading to the elimination of water and the formation of a thiazole-linked carboxylic acid. The reaction then proceeds through the protonation of the ion-dipolar intermediate, which is generated from the isocyanide **41** and ketones **42**. Finally, the carboxylate ion attacks the protonated site, and after acyl group rearrangement, the reaction affords the functionalized thiazolodepsipeptide **43**. The method exemplifies a sustainable, multicomponent strategy aligning with green chemistry principles through solvent recycling, a straightforward procedure without the need for added catalysts.

In 2017, Shahvelayati and co-authors[80] developed an efficient three-component tandem synthesis of a thiazole-based acetic acid derivative **47**, utilizing phenyl glycine **44**, aroylisothiocyanate **45**, and 4-methoxyphenacyl bromide **46** in the ionic liquid 1-methyl-3-pentylimidazolium bromide [mpim]Br as a green solvent. The experimental protocol proceeded at 50 °C for 1 hour, yielding the desired product in excellent yield



Scheme 19 Synthesis of thiazole using ionic liquid, [Bmim][OAc].

© 2025 The Author(s). Published by the Royal Society of Chemistry

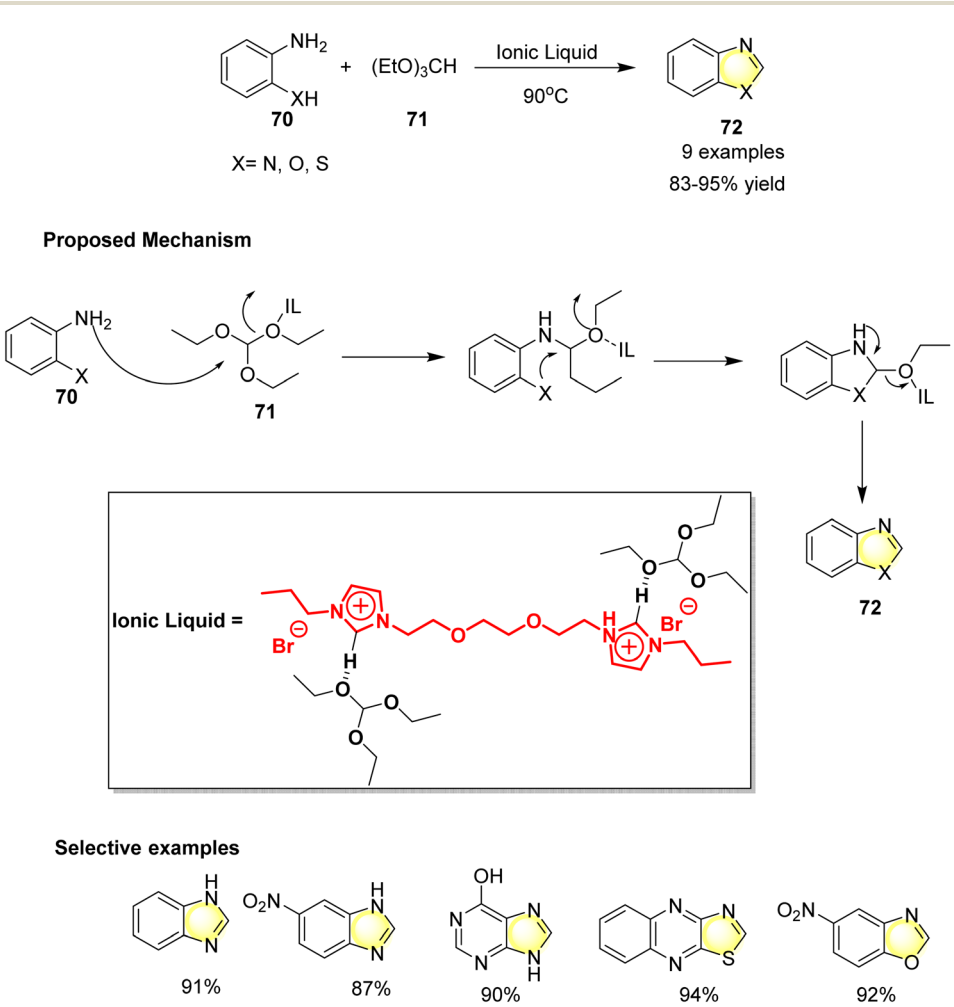
Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

(>97%). While the precise mechanism of the reaction remains unclear, a feasible explanation can be proposed for the observed product formation. The proposed reaction mechanism proceeds through the initial condensation of the phenyl glycine **44** with the aroylisothiocyanate **45**, yielding a thiourea intermediate **A**. Subsequent *S*-alkylation with the 4-methoxyphenacyl bromide **46** furnishes intermediate **B**, which undergoes intramolecular cyclization to generate intermediate **C**. Finally, dehydration (elimination of H_2O) from this intermediate leads to the formation of thiazole-based acetic acid derivative **47** (Scheme 14). Notably, [mpim]Br functions as an environmentally benign and recyclable solvent platform.

4.2. Task-specific and catalytic role (solvent + catalyst dual role)

In the year 2004, Nadaf and co-authors[81] introduced a novel one-pot, regioselective approach for synthesizing benzothiazoles **50** using substituted *o*-phenylenediamine **48** and substituted benzoyl chloride **49**, utilizing room-temperature ionic liquids (RTILs) as the reaction medium under ambient conditions. The researchers utilized imidazolium-based ionic liquids, namely [Hbim]BF_4 and [bbim]BF_4, which functioned simultaneously as solvents and promoters, thereby obviating the requirement for conventional acid catalysts (Scheme 15). The ILs not only enhanced the reaction rates but also enabled high yields and excellent selectivity. Among the tested ILs, [Hbim]BF_4 demonstrated the highest efficiency, likely due to its intrinsic Brønsted acidic nature. Furthermore, the ability to recycle the ionic liquids with minimal loss of catalytic activity highlights both the environmental as well as affordability and eco-friendly benefits offered by this green methodology. This investigation emphasizes both the catalytic and promoting functions of task-specific ionic liquids in heterocyclic synthesis, underscoring their promise as efficient, sustainable, and scalable media for organic transformations.

In 2008, Maradolla *et al.*[82] introduced a single-step, high-yield synthesis of benzthiazoles **53** using an ionic liquid, 1-butyl-3-methylimidazolium tetrafluoroborate [bmim]BF_4 as the reaction medium. In this protocol, various carboxylic acids **51** were directly condensed with substituted *ortho*-phenylenediamine derivatives **52** at elevated temperatures under ambient pressure (Scheme 16). The ionic liquid not only served



Scheme 20 Synthesis of thiazole using novel dicationic ionic liquid.

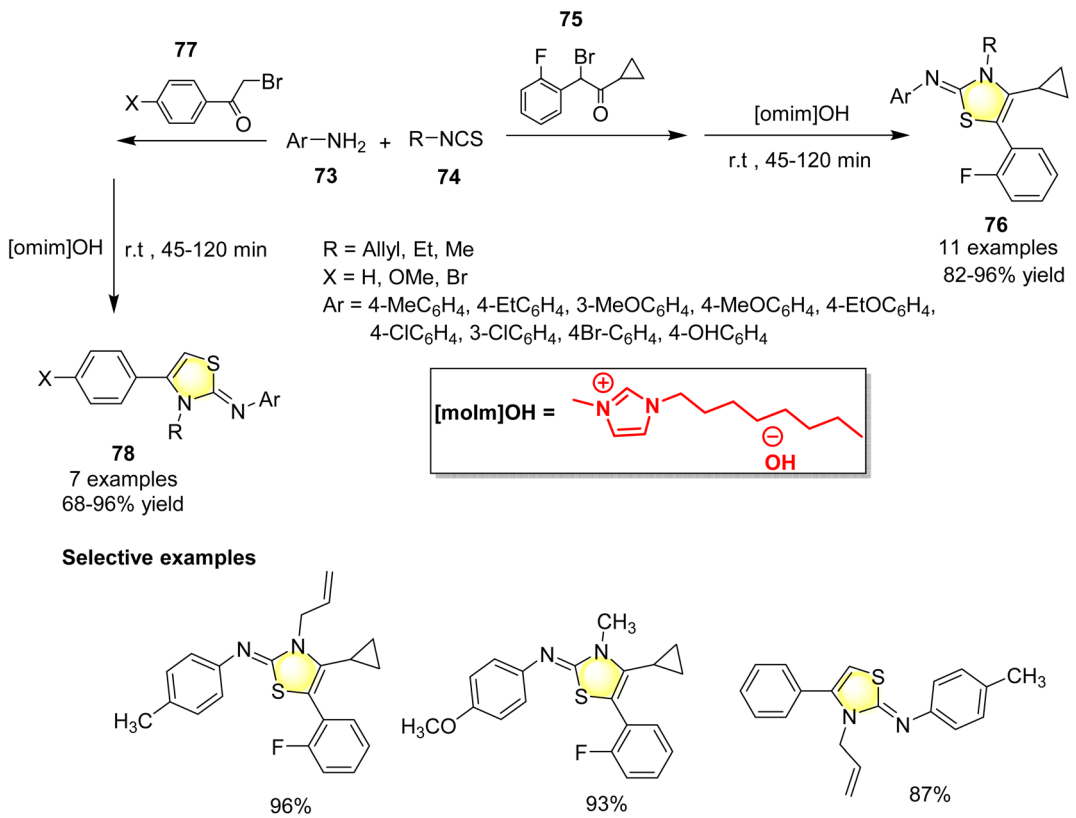
Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM. This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

as a green solvent but also promoted the reaction, achieving excellent yields (up to 96%) without the necessity for any external catalyst. The ionic liquid was reusable over multiple cycles with negligible decline in efficiency, and the method exhibited strong regioselectivity, broad substrate tolerance, and ease of operation. The study highlights the dual functionality of ionic liquids acting as both the medium and enhancer of the reaction, presenting a green and scalable strategy toward the construction of heterocyclic frameworks.

In 2012, Yadav *et al.*[83] described an innovative, high-yielding, and eco-conscious two-step synthetic approach for the preparation of fused thiazolo and benzothiazolo-pyrimidine compounds **61a–e**. The method involves the reaction of 2-aminothiazole **54** or 2-aminobenzothiazoles **55a–e** with Meldrum's acid **56**, in which the C-4 and C-6 sites are susceptible to nucleophilic substitution, while the C-5 position favors electrophilic addition, followed by treatment with trimethyl orthoformate **57**. The reaction was carried out in an inert nitrogen environment under controlled thermal conditions of 40 ± 2 °C, employing ionic liquid 1-butyl-3-methyl imidazolium bromide [BMIM]Br to yield thiazolo-2-amino **58**/benzothiazolyl-2-aminomethylene-1,3-dioxane compounds **59a–e** with excellent yield (Scheme 17). The final products were obtained *via* cyclization in 1-butyl-3-methylimidazolium tetrafluoroborate/triflate [BMIM]Br/OTf maintained at a moderate reaction temperature, affording yields of up to 88%. The ionic liquids were also shown to be recyclable over multiple cycles with only slight reductions in efficiency, demonstrating their potential as green reaction media for heterocyclic synthesis.

In the year 2015, Khillare *et al.*[84] developed a sustainable and single-step approach involving multiple components for synthesizing thiazole-substituted pyrazolyl-4-thiazolidinones **65a–r**. The reaction proceeds *via* the condensation of heterocyclic aldehydes as key starting materials **62a–f**, aromatic amines **63a–c**, and mercaptoacetic acid **64** with the aid of ionic liquid, diisopropylethylamine acetate (DIPEAc), at room temperature (Scheme 18). The ionic liquid displays dual-purpose activity as a medium and catalyst, significantly accelerating the reaction and producing excellent product yields (70–93%) within a short reaction time (15–30 minutes). The developed protocol is amenable to scale-up, avoids toxic solvents and severe reaction parameters while allowing for easy recovery and reuse of the ionic liquid, thereby enhancing its sustainability and green chemistry profile. The approach supports the synthesis of bioactive heterocycles with potential anti-inflammatory properties.

Concurrently, that year, Gao *et al.*[85] introduced a novel methodology aimed at producing benzothiazole-based compounds **69** through condensation with 2-aminothiophenols **66** with carbon dioxide **67** and triethoxysilane **68** under mild conditions at room temperature and low pressure (0.5 MPa), using acetate-based ionic liquid [bmim]OAc as the catalyst. This approach afforded the desired products in excellent yields, up to 99%. The ionic liquid [bmim]OAc functioned as a dual-acting catalyst by facilitating the activation of both CO_2



Scheme 21 Synthesis of thiazole using ionic liquid [omim]OH.

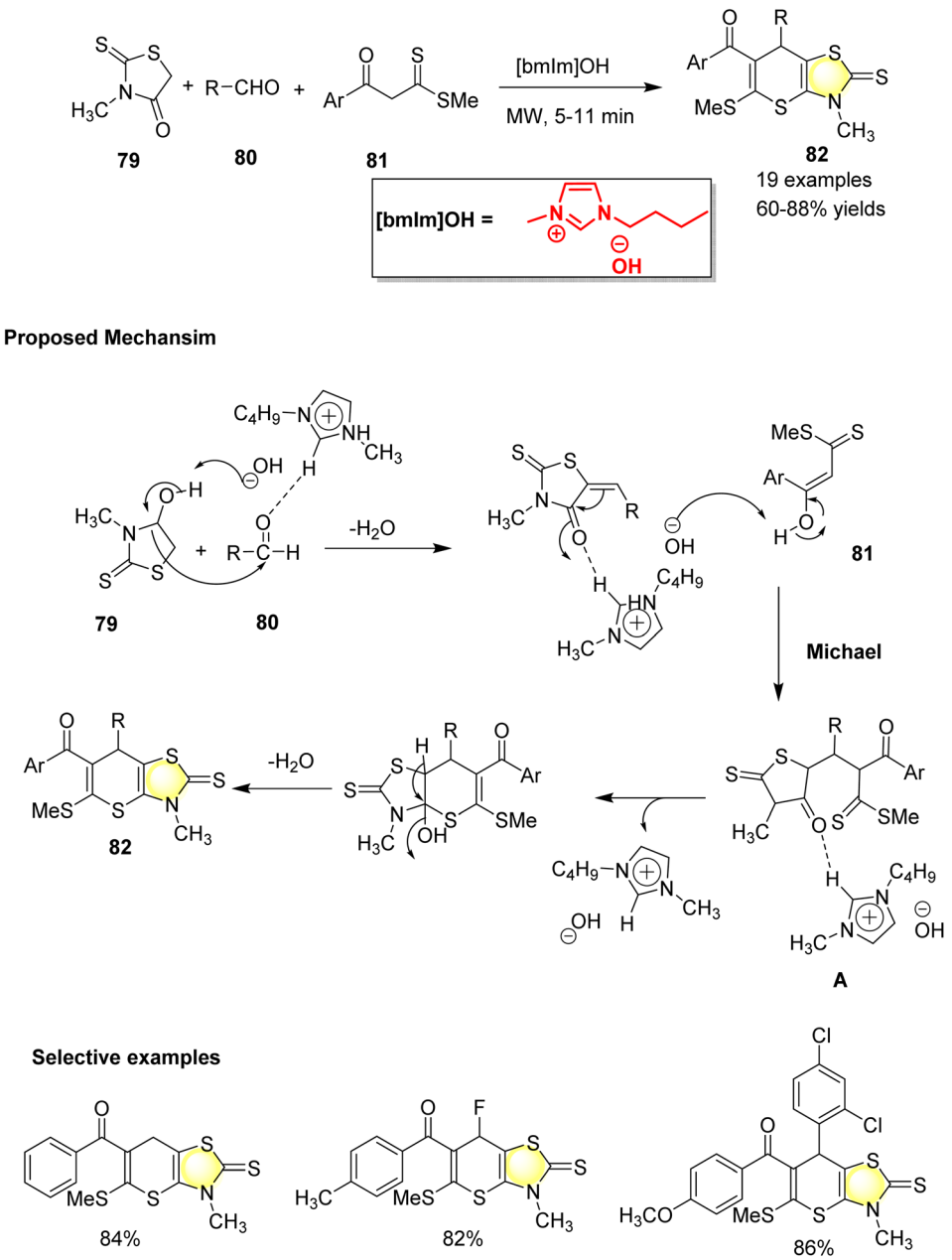
© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

and hydrosilane, which results in the production of a formoxysilane species, while also enhancing the reactivity of 2-aminothiophenols *via* hydrogen bonding, ultimately facilitating the formation of benzothiazoles.

Based on experimental observations and previous studies,[86–88] a plausible mechanism is outlined in Scheme 19. Initially, carbon dioxide **67** is activated by the ionic liquid (IL) to generate intermediate **A**. The IL also facilitates the activation of the Si–H bond in triethoxysilane **68**, promoting its insertion into **A** to yield the formoxysilane intermediate **C**. Concurrently, the anion ($[OAc]^-$) of the IL activates the o-substituted aniline **66** (X = NH, S) through hydrogen bonding, enabling the nucleophilic nitrogen atom to attack the carbon center of intermediate **C** and form intermediate **E**. Subsequent intramolecular cyclization and dehydration of **E** afford the benzothiazole-based compounds **69**.

To investigate the reaction mechanism, NMR analyses were performed on [Bmim][OAc] with carbon dioxide **67**, 2-aminothiophenols **66**, and triethoxysilane **67**. In the ^{1}H NMR spectra, the NH_2 and SH proton signals of 2-aminothiophenols **66** shifted downfield from δ 4.92 ppm to 6.39 ppm and δ 5.44 ppm to 6.62 ppm, respectively. Similarly, the acetate methyl proton signal moved from δ 1.56 ppm to 1.80 ppm, while the C–H signals of [Bmim][OAc] shifted slightly upfield. These chemical

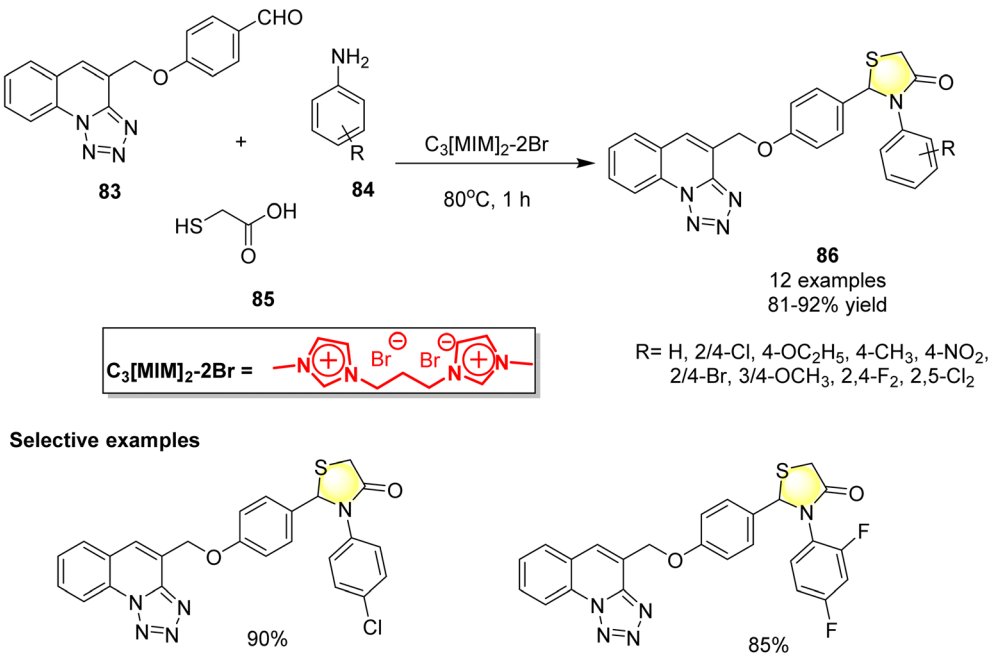


Scheme 22 Synthesis of thiazole using ionic liquid [bmim]OH.

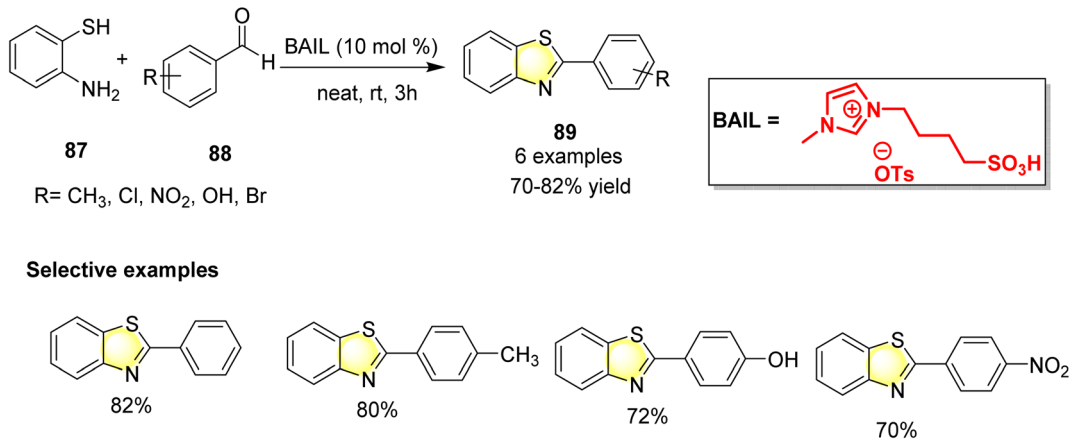
Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

shift changes confirm strong hydrogen-bonding interactions between the $[OAc]^-$ anion and the substrate. Since ionic liquids lacking $[OAc]^-$ exhibited no catalytic activity, these results suggest that hydrogen bonding with $[OAc]^-$ plays a crucial role in benzothiazole formation. This methodology provides a straightforward, non-metallic approach for the synthesis of benzothiazoles, with promising applications. This approach also promotes future C–S bond-forming methodologies utilizing CO_2 as a carbon source and ionic liquids (ILs) as catalytic media.

Later, Hasanpour and co-workers[89] reported a novel dicationic ionic liquid in 2015, which was employed as a catalyst for benzothiazoles **72** in the presence of *o*-phenylenediamines **70**, 2-aminothiophenol, 2-aminophenol, diaminopyrimidines, and triethyl orthoformate **71**. The reactions proceeded without employing any solvent, utilizing only a small quantity of the catalyst, and delivered the target products in good yields from 83–95%. A notable feature of this novel catalyst is the presence of an ethyleneoxy bridge, which enhances the capacity of the ionic medium to accommodate organic substrates. The methodology offers several advantages, including operational simplicity, high conversion efficiency, catalyst reusability, ease of product purification, and reduced reaction time. The catalytic role of the imidazolium-based ionic liquid involves substrate activation through hydrogen bonding. The acidic hydrogen atom of the imidazolium cation interacts with the oxygen atom



Scheme 23 Synthesis of thiazole using dicationic ionic liquid.



Scheme 24 Synthesis of thiazole using Brønsted acidic ionic liquid (BAIL-1).

© 2025 The Author(s). Published by the Royal Society of Chemistry

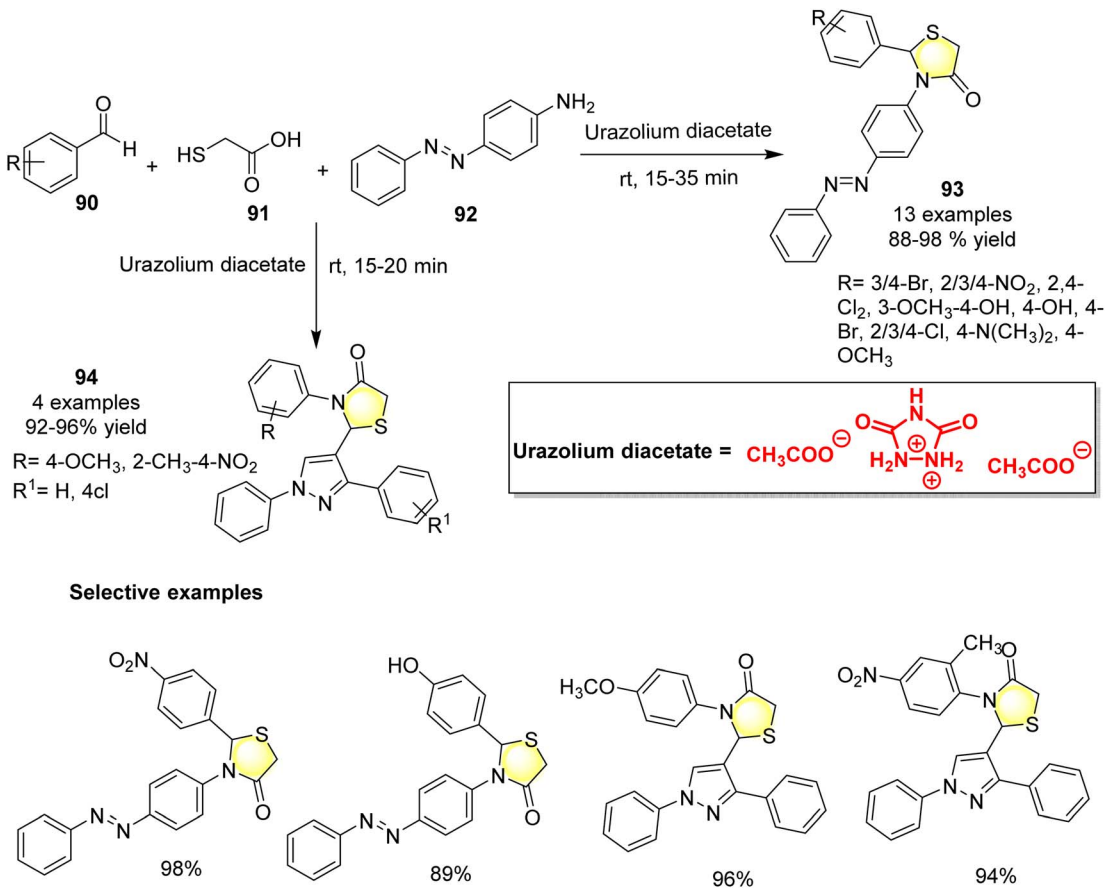
Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM. This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

of triethyl orthoformate **71**, forming a hydrogen bond.[90] This interaction increases the electrophilicity of the carbon centre in triethyl orthoformate **71**, facilitating its nucleophilic attack by *o*-phenylenediamine **70**, 2-aminophenol, or 2-aminothiophenol. The subsequent condensation produces the corresponding intermediate, which undergoes intramolecular cyclization and dehydration to yield the heterocyclic products such as benzimidazole, benzoxazole, or benzothiazole (Scheme 20).

The DFT calculations (RHF/6-31G level) further confirm this mechanism, showing hydrogen bond distances around 2.08 Å and bond angles near 157°, which validate the formation of a strong hydrogen bond with the oxygen atoms of triethyl orthoformate and aldehydes, enhancing the electrophilicity of the carbonyl carbon and promoting condensation. These DFT insights demonstrate that both hydrogen bonding and electrostatic interactions between the cation and substrate are key to the catalytic efficiency of the ionic liquid. The interaction between the ionic liquid and the substrate was further confirmed by ^{1}H NMR analysis. When [Bmim][OAc] was mixed with 2-aminothiophenol, the proton signals of the –NH_2 and –SH groups shifted downfield (from δ 4.92 → 6.39 ppm and δ 5.44 → 6.62 ppm, respectively). Similarly, the methyl protons of the acetate anion shifted from δ 1.56 → 1.80 ppm, while the C–H signals of the imidazolium cation moved upfield. These shifts indicate hydrogen-bonding between the $[OAc]^-$ anion and the substrate, enhancing electron deficiency at reactive sites and facilitating condensation and cyclization. The NMR evidence, together with DFT results, strongly supports the proposed mechanism, where the ionic liquid activates both the nucleophile $[OAc]^-$ and carbonyl component (imidazolium cation).

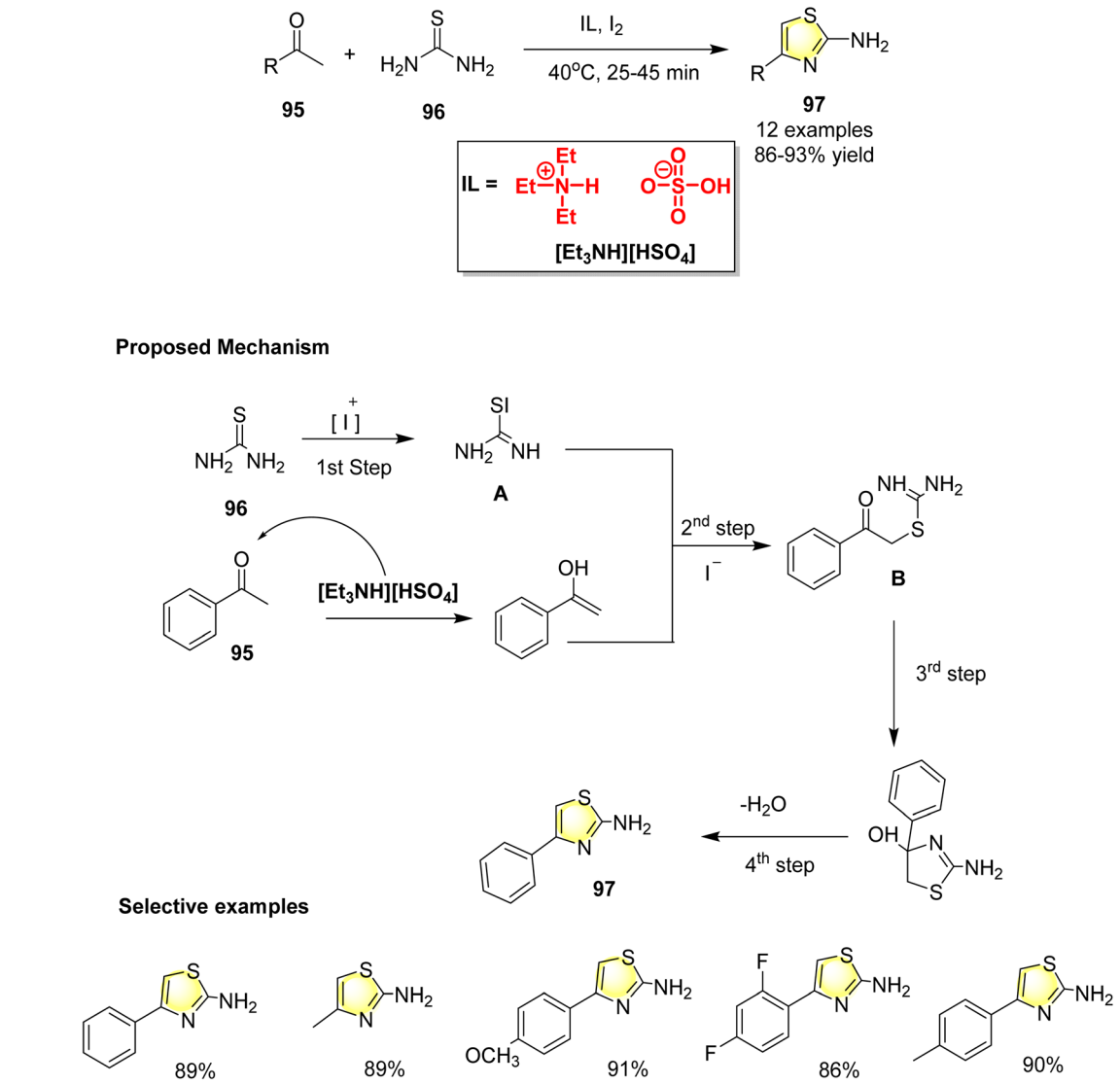
In 2016, Shiran and co-authors[91] introduced an efficient approach for synthesizing thiazol-2-imine derivatives through a regioselective, integrated one-pot approach using three starting materials. Their strategy utilized aryl amines **73**, alkyl isothiocyanates **74**, and substituted phenacyl bromides **75** to yield a variety of thiazole-based compounds, including fluorophenyl-substituted cyclopropyl thiazole derivatives **76a–k** and aryl-substituted allyl-imino thiazole derivatives **78a–o**. The reactions were executed in the presence of the ionic liquid 1-methyl-3-octylimidazolium hydroxide ([omim]OH), which served as both the solvent and base. The dual functionality of [omim]OH enabled regioselective product formation at ambient conditions, resulting in excellent yields (68–96%) (Scheme 21).

Again in 2016, Siddiqui *et al.*[92] outlined a sustainable and high-yielding synthetic method for the construction of thiazole-based thione-fused heterocycle derivatives **82a–n** through a single-vessel multicomponent process. The protocol utilizes the basic ionic liquid 1-butyl-3-methylimidazolium hydroxide ([bmim]OH) as both catalyst and solvent. This transformation was achieved through a reaction under microwave irradiation



Scheme 25 Brønsted acid-catalyzed synthesis of thiazole using urazolium diacetate.

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



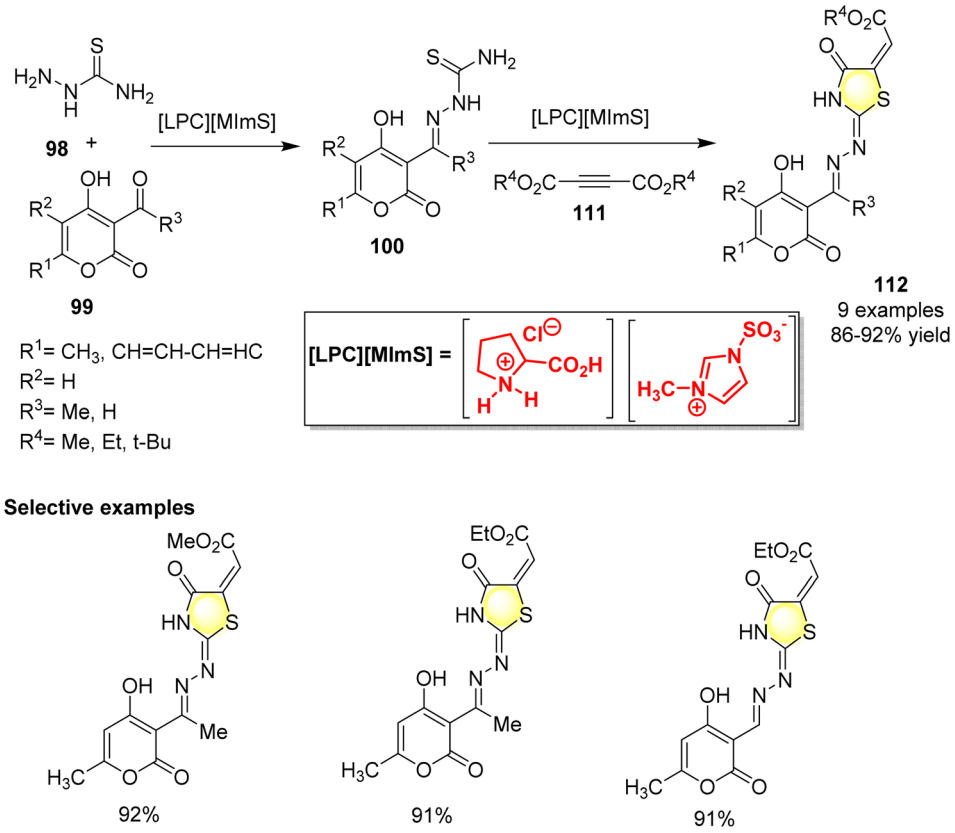
Scheme 26 Synthesis of thiazoles using ionic liquid $[Et_3NH][HSO_4]$.

involving methyl-substituted rhodamine **79**, substituted benzaldehydes **80a–n**, and aromatic dithiopropionate methyl esters **81a–n**, as illustrated in Scheme 22. Notably, the use of microwave irradiation enabled rapid reaction completion in the time range of 5–11 minutes, affording the desired products, providing excellent yields between 60–88%. The plausible reaction mechanism begins with the condensation of methyl-substituted rhodamine **79** and substituted benzaldehydes **80**, forming an α,β-unsaturated carbonyl compound, which subsequently acts as a Michael acceptor toward the aromatic dithiopropionate methyl esters **81**, producing an open-chain intermediate **A**. This intermediate undergoes regioselective intramolecular *S*-cyclization, leading to the construction of thiazole-based thione-fused heterocycle derivatives **82** in excellent yield. The observed regioselectivity can be attributed to the higher nucleophilicity of sulfur and the stabilizing influence of the imidazolium moiety, which favours *S*-cyclization over *O*-cyclization. The dual functionality of [bmim]OH significantly contributed to the enhanced reaction efficiency and sustainability of the process.

In 2019, Deshmukh and co-authors[93] employed a dicationic ionic liquid to facilitate the development of novel heterocyclic scaffolds, namely tetrazoloquinoline-linked thiazolidinone derivatives **86.** This transformation was achieved through a one-pot cyclocondensation reaction involving a freshly synthesized aldehyde **83**, aryl-functionalized amines **84**, and a sulfur-containing carboxylic acid **85** in polyethylene glycol as the reaction medium. With thermal activation of the mixture at 110 °C for 2 hours, the target products were isolated in moderate yields. The ionic liquid $[C_3(MIM)_2 \cdot 2Br]$ acted as both solvent and catalyst, offering a green, efficient alternative to traditional methods with excellent yields (81–92%) under mild conditions (Scheme 23). The synthesized thiazolidinone derivatives were analyzed *in vitro* for antitubercular activity against *Mycobacterium tuberculosis* H37Ra and *Mycobacterium bovis* BCG

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Scheme 27 Synthesis of thiazole using ionic liquid [LPC][MImS].

strains. Notably, **86a**, **86c**, and **86e** demonstrated notable inhibitory effects, with **86e** exhibiting the most pronounced potency. Additionally, molecular docking analyses indicated that these molecules showed strong binding affinities toward the DprE1 enzyme, a well-established target in tuberculosis therapy. These findings support the potential of these quinoline–tetrazole–thiazolidinone hybrids as promising leads for antitubercular drug development, highlighting the dual advantage of ionic liquid catalysis and molecular hybridization in medicinal chemistry.

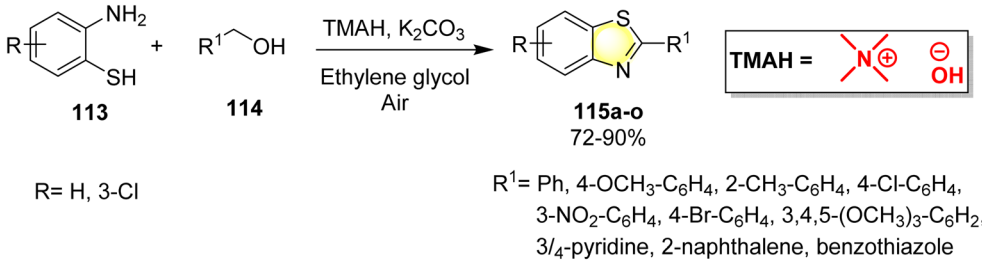
In 2020, Satyajit Pal and co-authors[94] established a clean and practical synthetic route to benzothiazole **89**, which was accomplished without the use of conventional solvents, utilizing an ionic liquid exhibiting Brønsted acidity (BAIL-1). This approach involves the reaction of 2-aminothiophenol **87** with benzaldehyde **88** under neat conditions at ambient temperature. The use of BAIL-1 not only eliminates the need for solvents but also facilitates the formation of the desired products in good yields ranging from 70–82%. The current methodology aligns with green chemistry principles and exhibits a broad and versatile substrate scope (Scheme 24). The Brønsted acidic ionic liquid (BAIL-1) functions not only as a solvent but also as a catalyst, performing an active role that enhances the efficiency of the condensation reaction.

Within the same time frame, Fekri *et al.*[95] outlined urazolium diacetate, a novel Brønsted dicationic acid, was employed as an effective catalyst in the preparation of novel azo dispersive dyes **93** and pyrazolyl derivatives **94** bearing a thiazolidine-4-one scaffold. The reaction proceeded *via* a solvent-free multicomponent approach involving diverse aldehyde substrates **90**, mercaptoacetic acid **91**, and *p*-amino azobenzene **92**, affording the target compounds in good yields, 88–98%. This approach has the advantage of being relatively inexpensive, non-toxic, easy to handle, environmentally friendly, and reusable (Scheme 25).

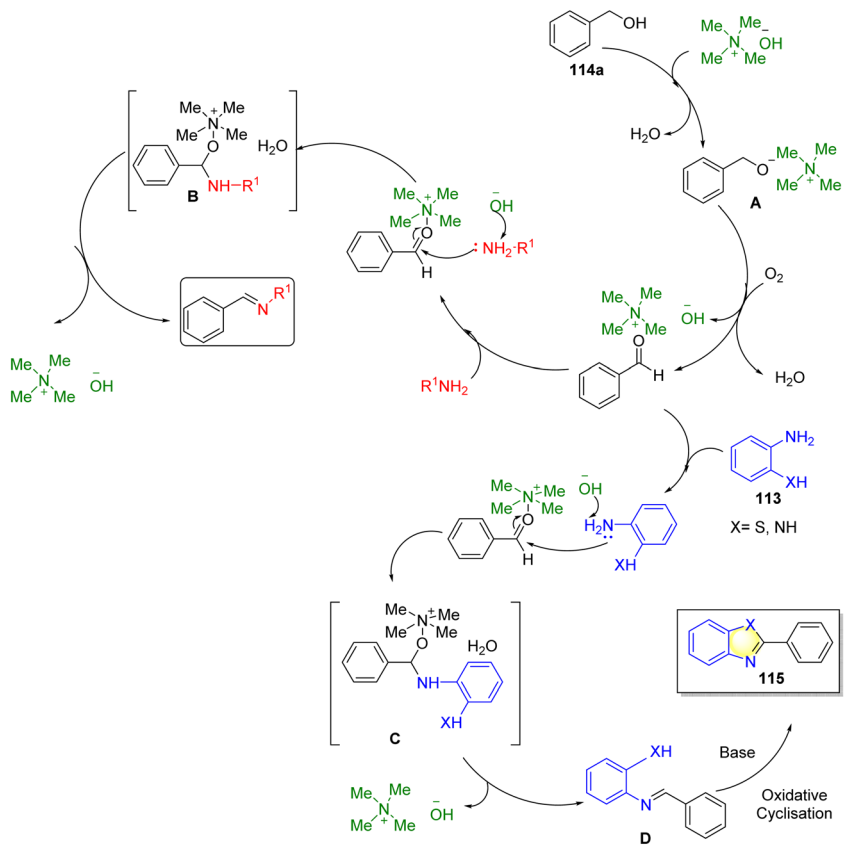
In 2021, Kakati *et al.*[96] established an eco-friendly, metal-free approach for synthesizing biologically active heterocycles such as 1,2,3,4-tetrahydropyrimidines, 2-aminothiazoles, and quinazolinones, using readily available ammonium-based ionic liquids, specifically triethylammonium hydrogen sulfate [Et_3NH][HSO_4]. The intended product, 2-aminothiazoles **97**, is formed *via* the reaction of acetophenone **95** and thiourea **96** with iodine. These ionic liquids functioned as recyclable Brønsted acid catalysts, facilitating single-step multicomponent transformations under gentle and solventless conditions (Scheme 26).

A feasible reaction pathway begins with the iodine-assisted oxidation of thiourea **96**, generating a thiyl electrophilic species **A**. The acetophenone **95** then undergoes acid-catalyzed enolization, and the resulting enol intermediate reacts with species **A** through an α-sulfenylation process, affording the α-sulfur-substituted ketone **B**. Subsequent intramolecular

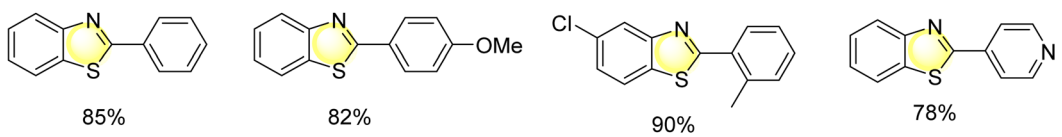
Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Proposed Mechanism



Selective examples



Scheme 28 Synthesis of thiazole using an ionic liquid, (TMAH).

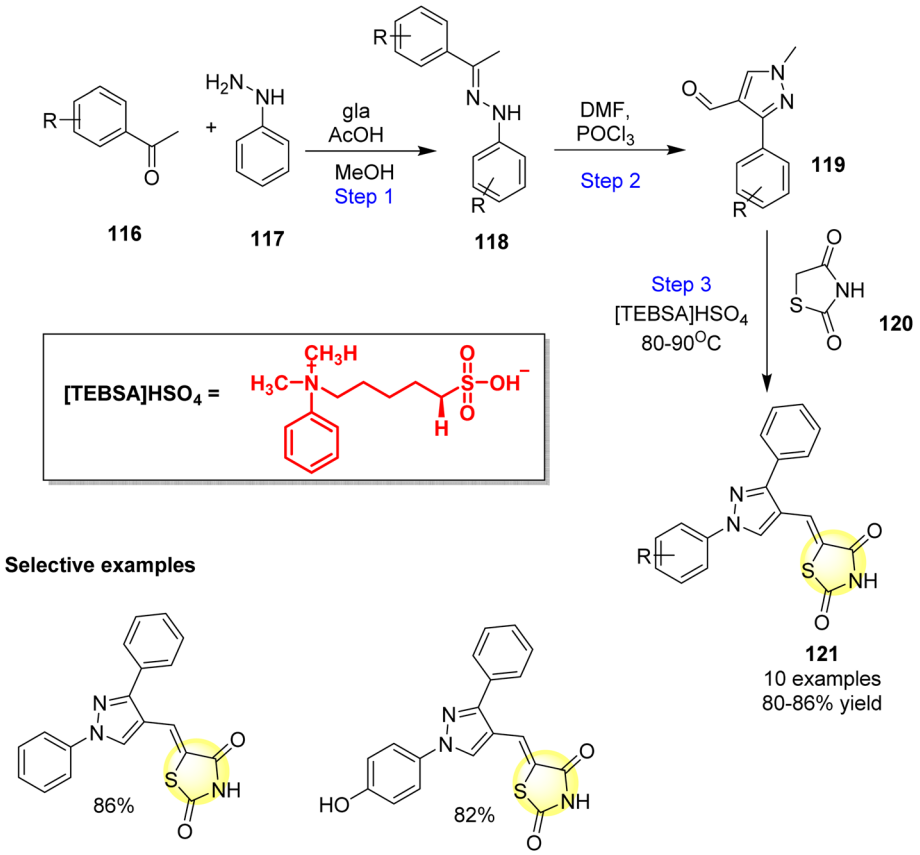
nucleophilic addition of the imine nitrogen to the carbonyl carbon produces intermediate **C**, which, upon dehydration, yields the desired 2-aminothiazole derivative **97**.

The methodology provided high product yields, accommodated a wide range of substrates, and allowed for straightforward product isolation. This work demonstrates the applicability of ionic liquids as eco-friendly media and Brønsted acid catalysts in the efficient construction of biologically active heterocyclic scaffolds.

In the same year, Mirakmahaleh *et al.*[97] introduced an expedient, solvent-free, tandem reaction of novel antibacterial hydrazono-4-thiazolidinone derivatives **112** in 2021. A naturally derived binary ionic liquid system, consisting of L-prolinium chloride (LPC) and 1-methylimidazolium-3-sulfonate (MImS),

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



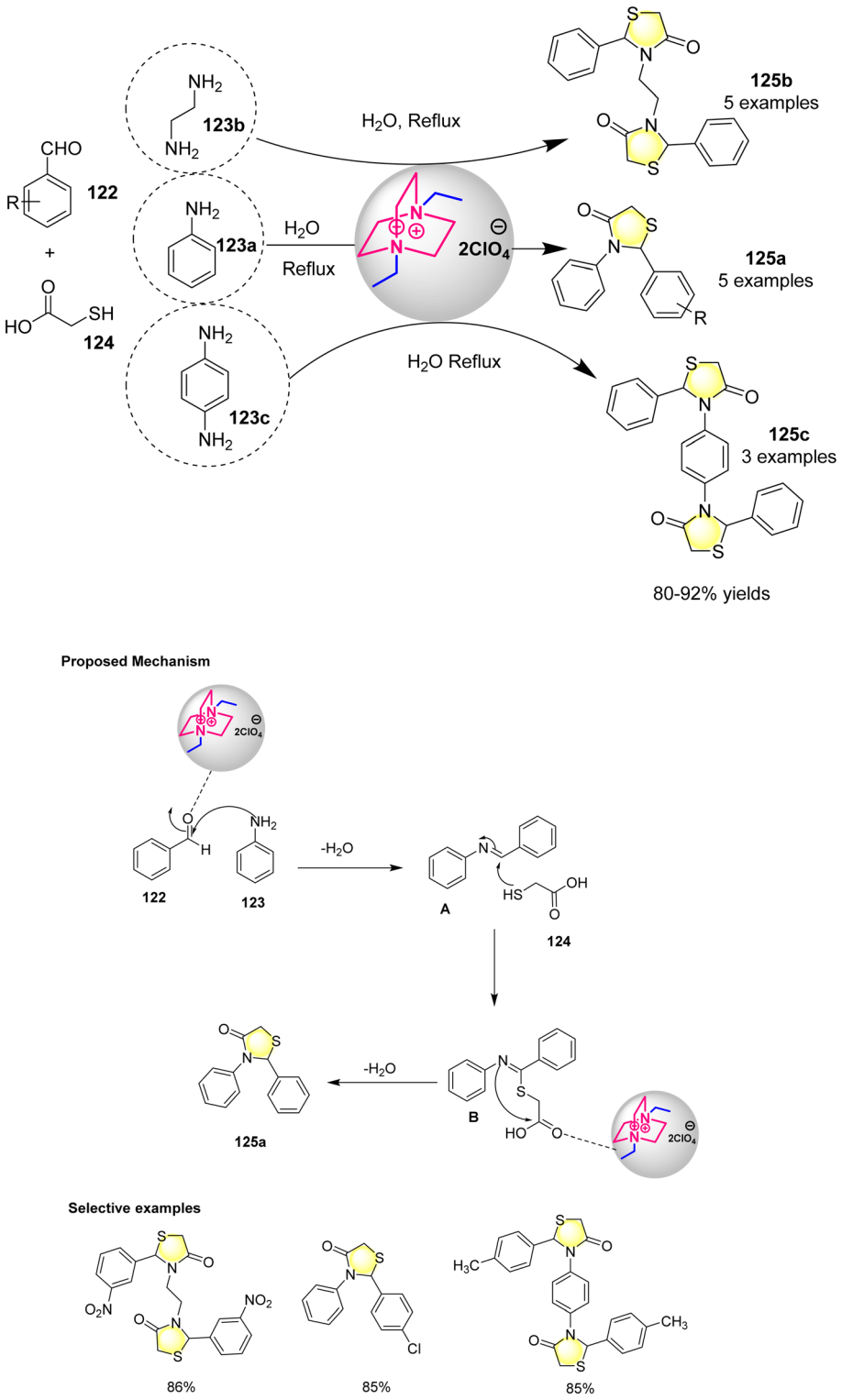
Scheme 29 Synthesis of thiazole using an ionic liquid [TEBSA]HSO_4.

was employed as a catalytic facilitator for the generation of thiazolidinone derivatives bearing hydrazone moieties bearing methylidene-substituted pyrone and chromone scaffolds. The reaction pathway involved an initial condensation between hydrazine thiocarboxamide **98** and acylated 4-hydroxypyrone scaffold **99**, forming the hydrazone-based reactive intermediate **100**. Subsequent condensation of intermediate **100** with acetylenic esters **111** led to the construction of the target products **112** in excellent yields ranging from 86% to 92%. The binary ionic liquid not only exhibited higher catalytic performance than its components but also showed good air and moisture stability and reusability over multiple cycles (Scheme 27).

In the [L-prolinium chloride] [1-methylimidazolium-3-sulfonate] ([LPC][MImS]) catalytic system, substrate activation primarily arises from hydrogen-bonding and electrostatic effects. The protic centres of L-proline (NH_2^+ and COOH) together with the counter anions (Cl^- and SO_3^-) form strong hydrogen bonds with the substrate's carbonyl oxygen, resulting in polarization of the C=O bond and enhancing its susceptibility to nucleophilic attack by thiosemicarbazide. The ^{1}H NMR spectrum exhibits a broad resonance at δ 8.27 ppm, attributed to the exchangeable NH_2^+/COOH protons, indicating extensive hydrogen bonding, while the methine signal at δ 4.11 ppm (dd, J = 8.4, 6.8 Hz) reflects dipolar coupling within the proline framework. DFT calculations at the UM06-2X/6-311++G(d,p) level showed that the energy difference between tautomeric and atropoisomeric forms is less than 2 kcal mol^{-1}, implying rapid interconversion and stabilization through electrostatic interactions in the ionic phase. Additionally, IR spectra revealed broad O–H/N–H stretching vibrations (3438–3158 cm^{-1}) and C=O absorptions (1680–1730 cm^{-1}), confirming hydrogen-bond-assisted activation. Collectively, these findings suggest that [LPC][MImS] acts as a bifunctional catalyst, providing an acidic, ionic, and hydrogen-bonding environment that stabilizes reactive intermediates and lowers the overall activation barrier. Notably, several of the synthesized thiazolidinone derivatives demonstrated encouraging antibacterial activity, underscoring their potential in drug discovery.

Subsequently, Badhani *et al.*[98] presented a sustainable, metal-free approach was developed to construct a range of heterocyclic frameworks enriched with nitrogen and sulfur atoms **115** using tetramethylammonium hydroxide (TMAH) as a catalytic ionic liquid. This protocol employs atmospheric oxygen as a green oxidant and efficiently promotes oxidative coupling between amines **113** and alcohols **114**. The method enables the construction of diverse heterocycles, facilitating the construction of heterocycles such as imines, benzimidazoles, benzothiazoles, quinoxalines, and quinolines through carbon–nitrogen, carbon–sulfur, and carbon–carbon bond formations (Scheme 28). The transformation occurs smoothly under gentle conditions, demonstrating wide substrate tolerance toward aromatic, aliphatic, and nitrogen-containing aromatic amines,

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



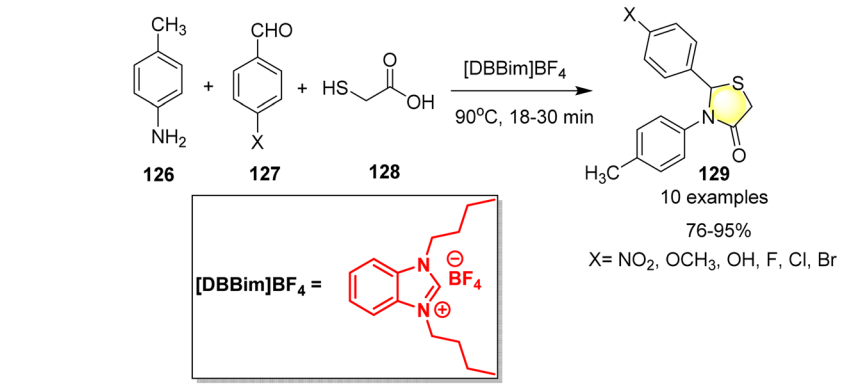
Scheme 30 DBAIL-promoted green synthesis of thiazole derivatives.

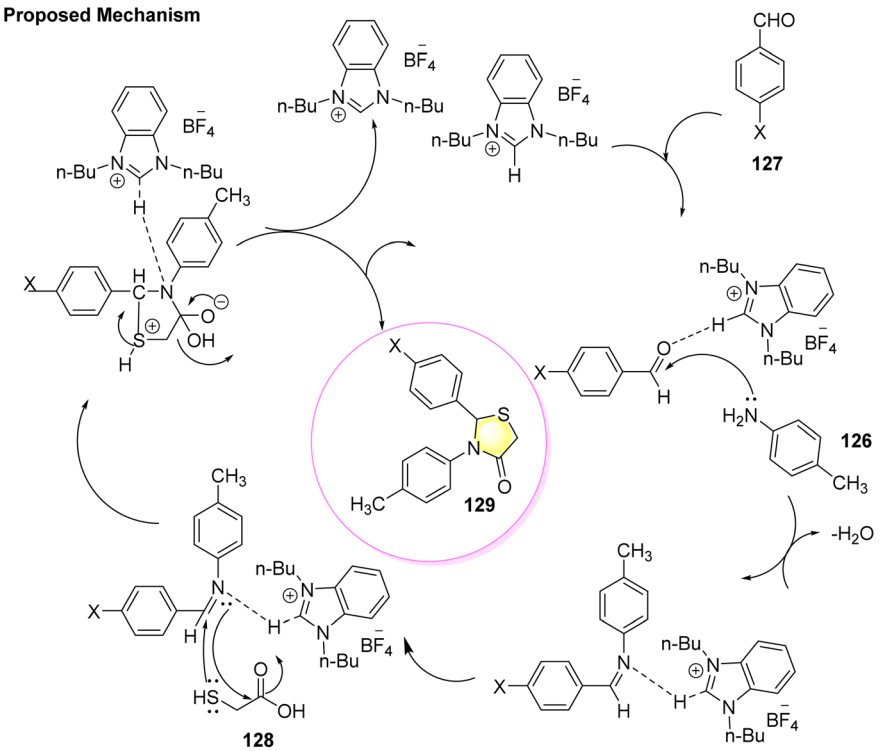
along with a variety of benzylic and heteroaryl alcohols. Mechanistic studies suggest the reactions follow an ionic pathway facilitated by aerobic oxidation.

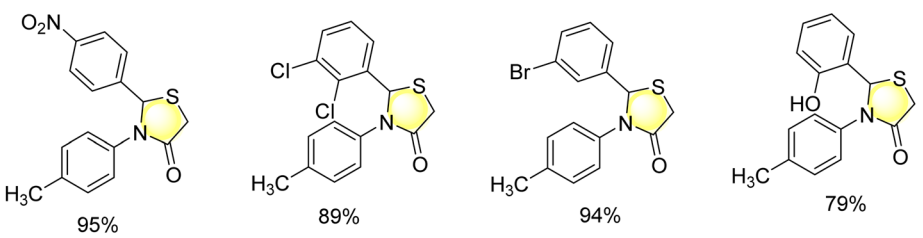
Initially, alcohol **114** reacts with TMAH to form an intermediate **A**, which is oxidized under aerobic conditions to benzaldehyde. The condensation of benzaldehyde with amines **113** produces the corresponding imine derivatives *via* intermediate **B**. Similarly, *in situ*-generated benzaldehyde can react with o-substituted aromatic amines to form intermediate **C**, which eliminates TMAH to give the imine species **D**.

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.





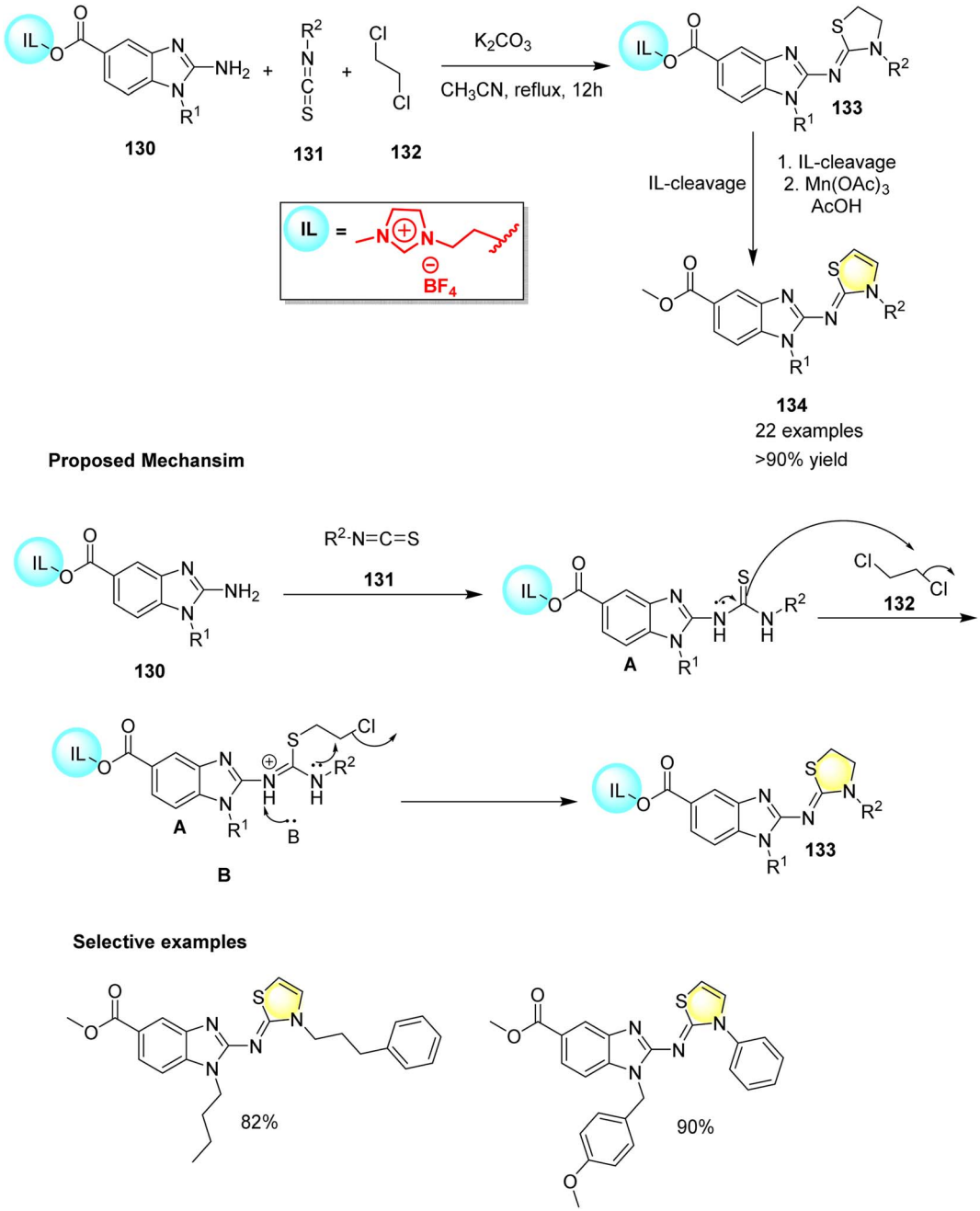


Scheme 31 Synthesis of thiazole using an ionic liquid [DBBim]BF_4.

Subsequent oxidative cyclization of **D** furnishes the target heterocyclic products **115**. This work presents a unified, sustainable approach to constructing diverse heterocycles, aligning in alignment with green chemistry guidelines, offering significant potential for pharmaceutical and industrial applications.

In 2023, Sowbhagyam *et al.*[99] established a green and efficient synthetic route was established towards the development of pyrazole-linked thiazolidinedione derivatives **121a–i** through

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



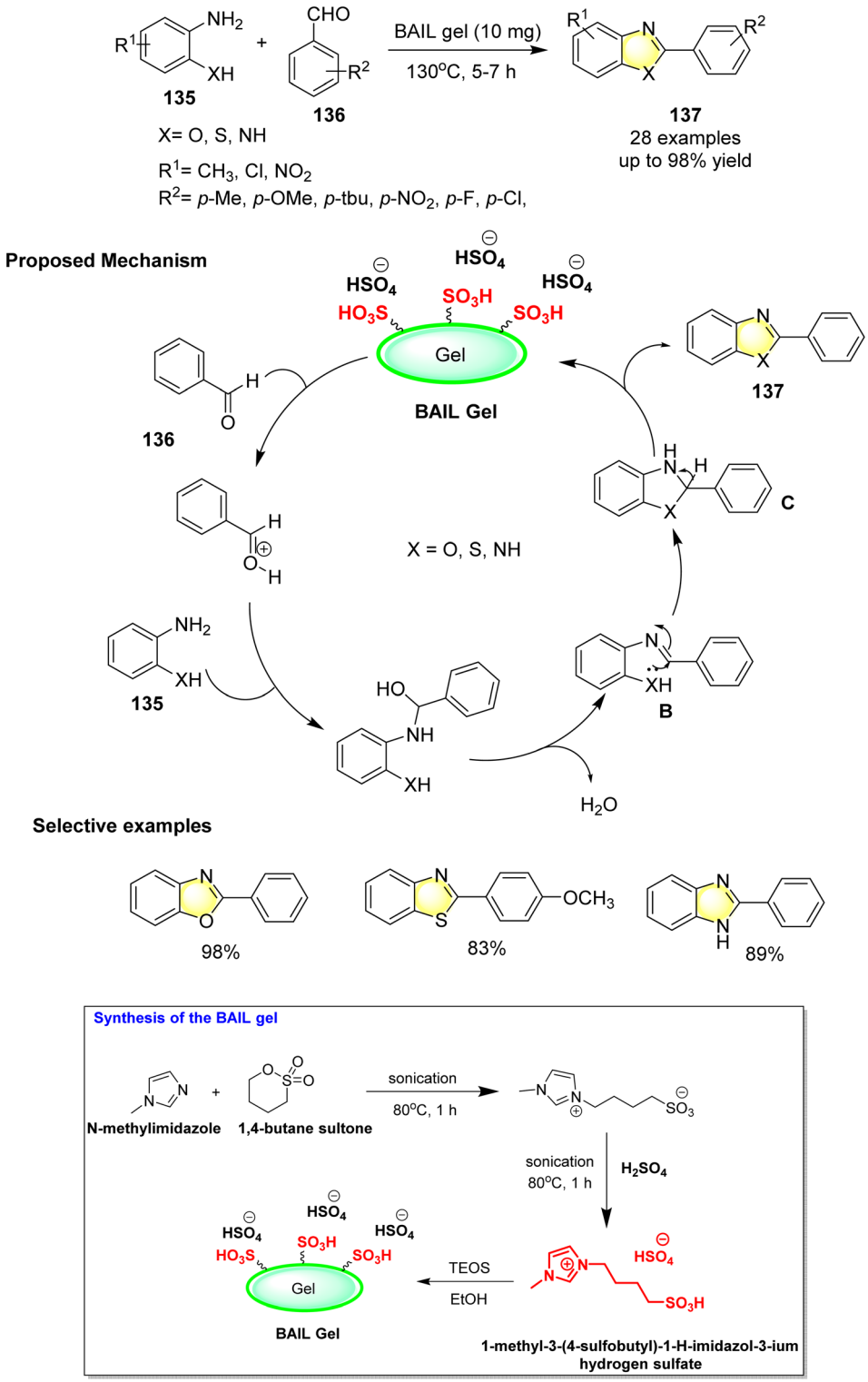
Scheme 32 Synthesis of thiazole using novel ionic liquid-tagged aminoethyl-functionalized imidazolium salt.

a sequence of three consecutive transformations. In the first step, aryl ethylidene phenyl hydrazine derivatives **118** were formed through condensation reactions involving acetophenone derivatives **116** with benzene-linked hydrazine derivative **117** in methanol, using acetic acid as a catalyst under reflux. These intermediates were then treated with the Vilsmeier–Haack reagent at room temperature for 8 hours to yield pyrazole-derived aromatic aldehydes **119**. The final step involved a Claisen–Schmidt condensation between compounds **119** and thiazolidine-2,4-dione **120**, in the presence of [TEBSA][HSO_4] as both a solvent and Brønsted acid catalyst (Scheme 29). The reaction was conducted *via* both traditional and microwave-assisted protocols, with microwave-assisted synthesis offering superior yields (up to 86%) and significantly reduced reaction times (8 minutes). The obtained molecules were tested for cytotoxic effects on SiHa, MDA-MB-231, and PANC-1 human cancer cell lines. Notably, **121c**, **121g**, and **121h** exhibited strong cytotoxic activity. The methodology demonstrates a sustainable IL-mediated protocol combining high efficiency with pharmacological relevance.

In the same year, Priyanka Pinate and Sangita Makone[100] reported a novel DABCO-derived protic acid-supported ionic

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



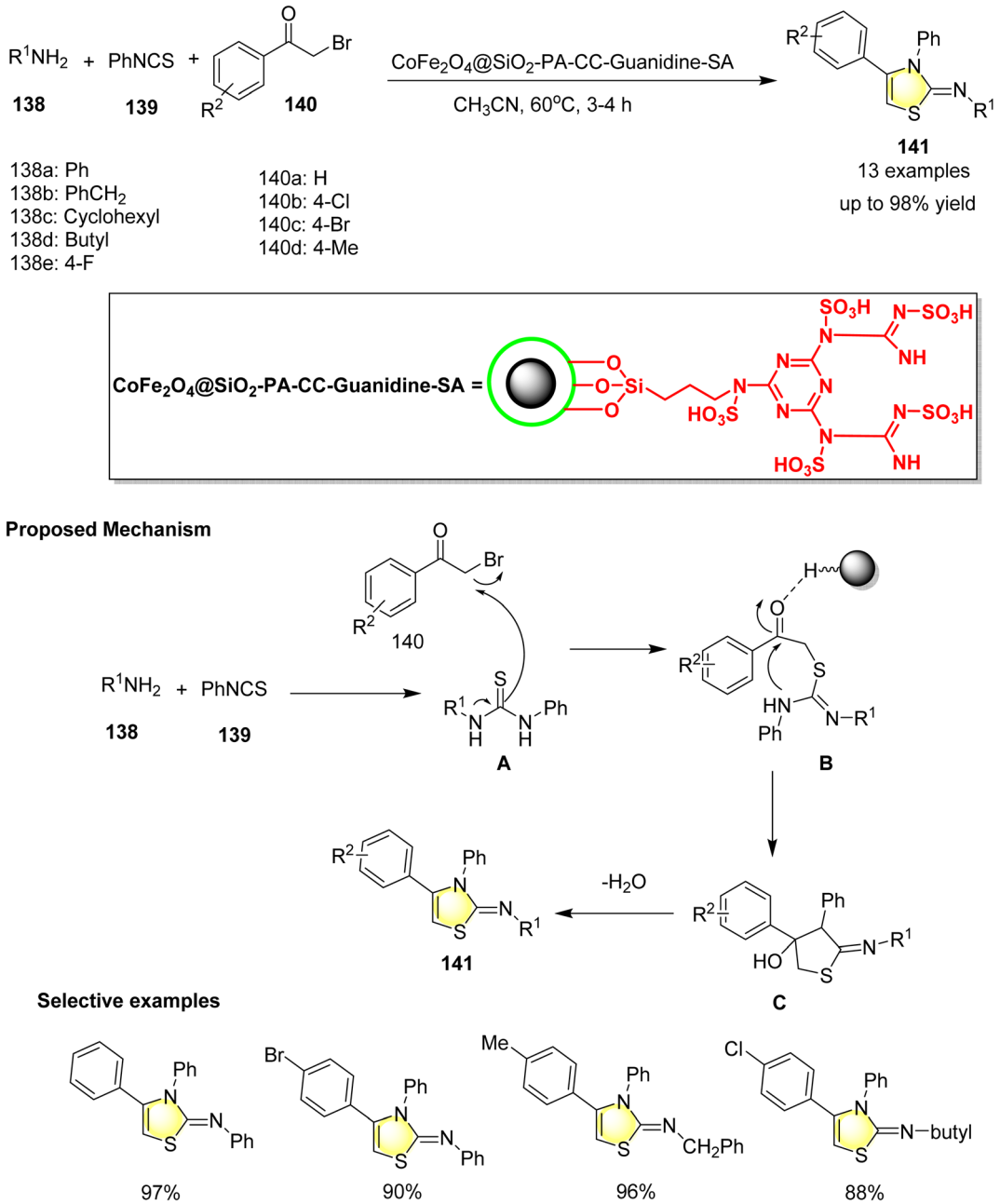
Scheme 33 Synthesis of thiazole using Brønsted acidic ionic liquid gel (BAIL gel).

liquid, $[C_4H_{10}\text{-DABCO}][ClO_4]_2$, serving as a potent, economical, and reusable catalyst towards the construction of thiazolidinone derivatives **125a–c**. The reaction was carried out in water, involving the condensation of various aldehydes **122**, modified with a combination of electron-rich and electron-deficient groups, exhibiting amines **123a–c** and thioglycolic acid **124**. This eco-friendly protocol afforded the desired thiazolidinone products in moderate to excellent yields, ranging from 80–92% with high purity. The proposed mechanism for synthesizing thiazolidin-4-one derivatives using the DABCO-based bifunctional acidic ionic liquid $[C_4H_{10}\text{-DABCO}][ClO_4]_2$ is shown in Scheme 30. The coordination of various aldehydes **122** with the

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

ionic liquid activates the carbonyl group, facilitating imine formation (intermediate **A**). The sulfur atom of thioglycolic acid **124** then attacks the amines **123** to form intermediate **B**, which undergoes ionic-liquid-assisted intramolecular cyclization and dehydration to yield thiazolidinone derivatives **125**. The ionic liquid featuring DABCO as a bifunctional acidic core (DABIL) demonstrated excellent reusability, maintaining its catalytic performance over five consecutive cycles. Furthermore, a set of five synthesized thiazolidinone analogues was screened for anticancer efficacy on MCF-7 cells using the MTT assay, showing moderate to notable cytotoxicity.

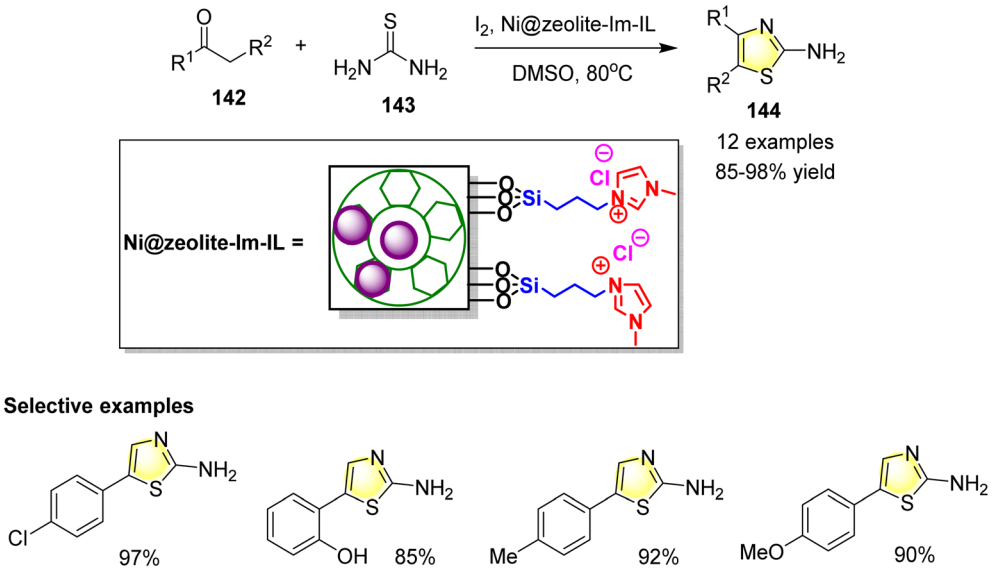
In 2024, Ahmad *et al.*[101] reported an environmentally friendly and streamlined one-pot, three-component method to synthesize thiazolidinone derivatives **129**, utilizing aldehydes bearing substituent groups **126**, *p*-methyl aniline **127**, and mercaptoacetic acid **128**. The reaction was carried out in the presence of a task-specific ionic liquid, 1,3-dibutyl-1*H*-benzo[*d*]imidazole-3-ium tetrafluoroborate [DBBim]BF_4, which functioned dually as both catalyst and solvent. This protocol enabled the rapid formation of thiazolidine derivatives within 18 to 30 minutes, affording moderate to high yields, typically from 76% to 95%.



Scheme 34 Synthesis of thiazole using $COFe_2O_4$@SiO_2-PA-CC-guanidine-SA as a magnetic nano catalyst.

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Scheme 35 Synthesis of thiazole using Ni@zeolite-Y-supported imidazolium ionic liquid.

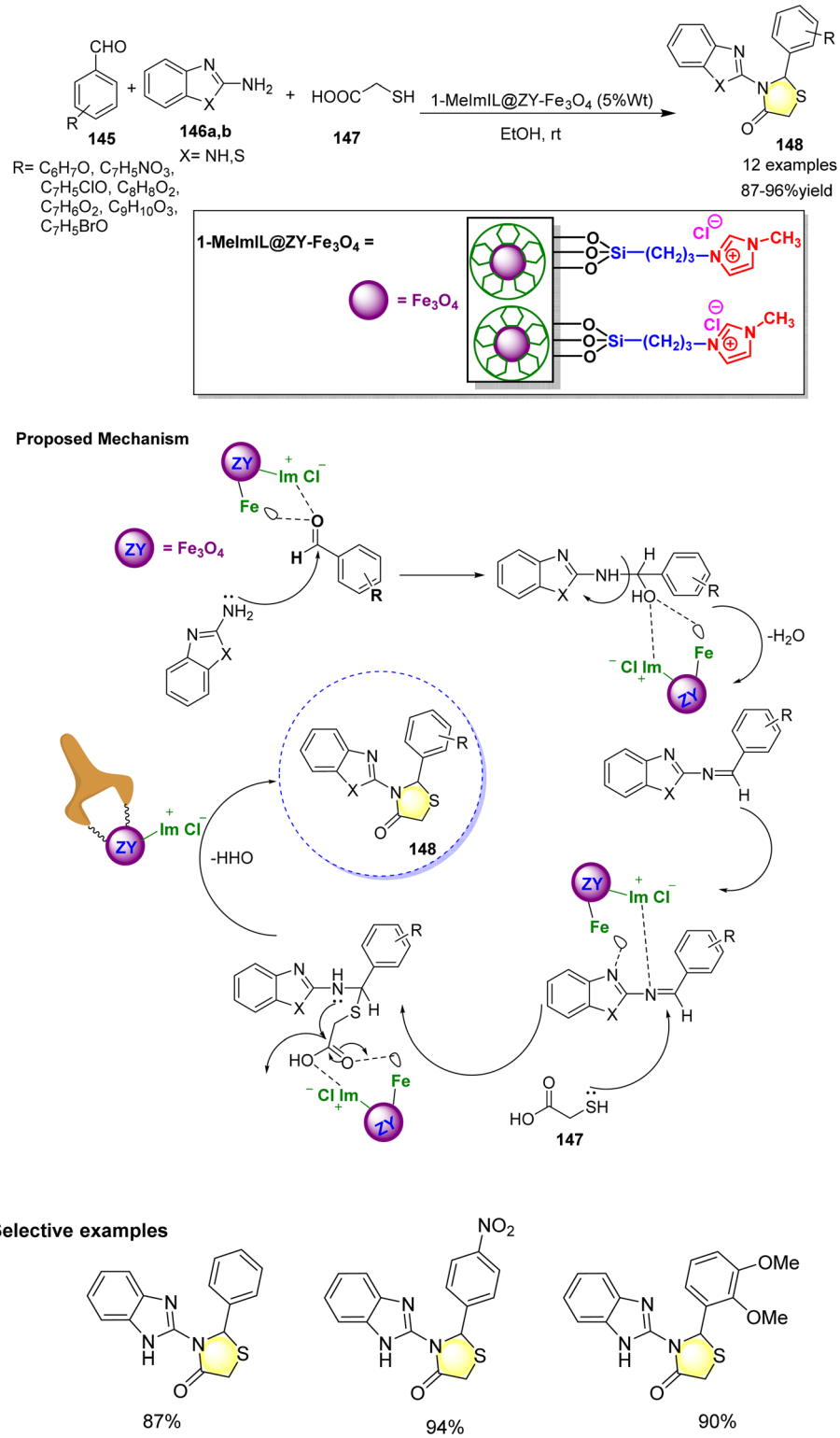
The proposed mechanism for thiazolidinone synthesis using the novel [DBBim]BF_4 ionic liquid is illustrated in Scheme 31. The benzimidazolium N–CH–N hydrogen forms hydrogen-bonding interactions with the aldehyde **126** carbonyl oxygen and the BF_4^- fluorine, increasing the electrophilicity of the carbonyl carbon. This activation promotes nucleophilic attack by *p*-methyl aniline **127**, followed by water elimination to form the imine intermediate. The imine then reacts with mercapto-acetic acid **128**, forming a C–S bond, and undergoes intra-molecular cyclization. Finally, dehydration yields the thiazolidinone derivatives **129**. Additionally, the protocol offers several advantages, including high conversion efficiency, cost-effectiveness, and the ability to proceed in the absence of solvents and without employing hazardous chemicals. This promising activity, combined with reduced reaction time, results in excellent catalytic activity.

4.3. Supported immobilized or non-hybrid ionic liquid system

In 2016, Chan-Yu-Chen *et al.*[102] present a sustainable and efficient approach to the synthesis of 2-imino-thiazolidine derivatives **133** and 2-imino-thiazolines derivatives **134** through a single-step, three-component process employing a soluble ionic liquid (IL) as the reaction medium. This methodology combines primary amines **130**, isothiocyanates **131**, and α-haloketones **132** employing a unique ionic liquid-tagged aminoethyl-functionalized imidazolium salt (Scheme 32). The IL acts as a reaction medium and a support, enabling efficient product formation and simple purification through extraction, avoiding traditional chromatography or recrystallization steps. The system exhibits a broad substrate scope, operates under optimized, non-severe conditions, and achieves satisfactory to excellent yields (72–92%). Additionally, the ionic liquid-supported amine catalyst was readily recoverable and retained its catalytic efficiency across several reuse cycles, emphasizing the sustainability and green nature of the developed method. According to the reported literature,[103] the proposed mechanism for the formation of 2-imino-1,3-thiazolidine derivatives **133** is illustrated in Scheme 32. Initially, the reaction between primary amines **130** and isothiocyanates **131** leads to the generation of an isothiourea intermediate **A**. Subsequent base-mediated abstraction of the acidic NH proton, positioned between the benzimidazole moiety and the thiourea carbonyl group, promotes a nucleophilic attack of the sulfur atom on the α-haloketone **132**, resulting in intermediate **B**. Finally, the base-assisted removal of the NH proton facilitates an intramolecular nucleophilic attack by the nitrogen atom on the C–Cl bond, yielding the 2-imino-thiazolidine derivatives **133**. This work makes a substantial contribution to green chemistry by integrating ionic liquid technology with multicomponent reactions (MCRs), thereby streamlining synthetic processes and minimizing chemical waste.

In 2019, Nguyen *et al.*[104] first introduced a green and effective strategy toward the construction of benzothiazoles **137** using a heterogeneous Brønsted acidic ionic liquid gel (BAIL gel), through the reaction of 1-methyl-3-(4-sulfobutyl)-1*H*-imidazolium hydrogen sulfate with tetraethyl orthosilicate (TEOS). This protocol entails the reaction of 2-aminothiophenol **135** with a broad range of aromatic aldehydes **136**, affording benzothiazoles in high to excellent yields, with some reaching up to 98%. Notably, the BAIL gel catalyst demonstrated excellent reusability, maintaining catalytic performance over five consecutive cycles (Scheme 33). In agreement with previous literature and our experimental findings, the BAIL gel plays a crucial role in facilitating the reaction mechanism. Initially, the carbonyl oxygen of the aromatic aldehyde **136** undergoes protonation *via* the $-SO_3H$ functional sites present on the catalyst surface. This activation enables the condensation of the aromatic aldehyde

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

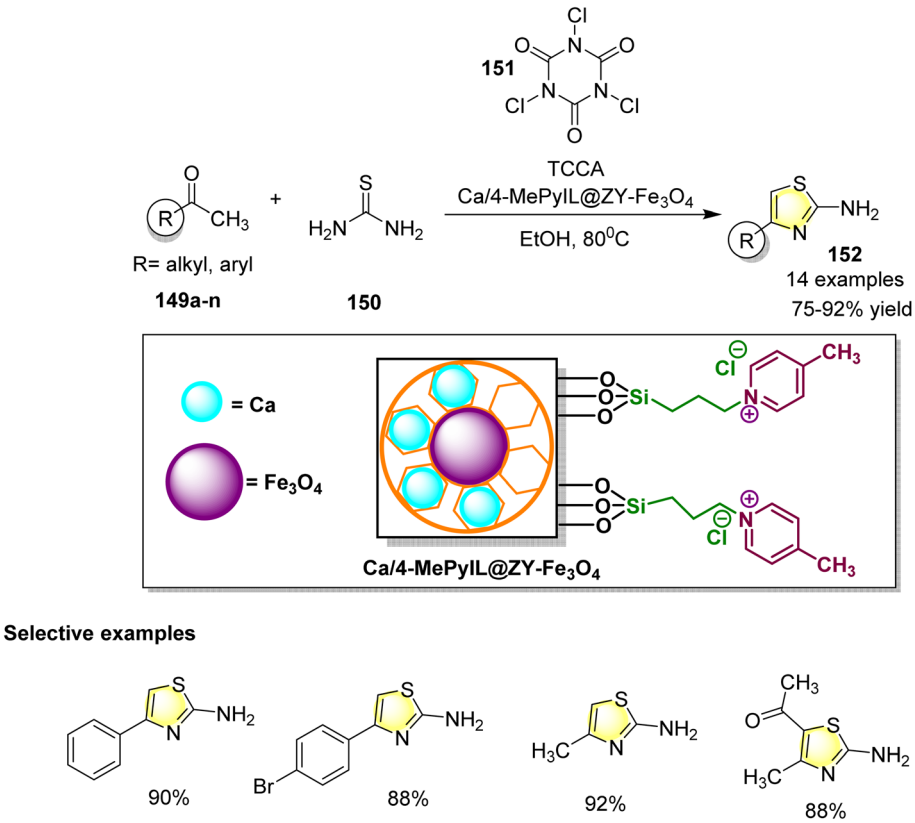


Scheme 36 Synthesis of thiazole using Fe_3O_4@Zeolite-Y functionalized with *N*-methylimidazolium ionic liquid.

136 with 2-aminothiophenol **135**, forming intermediate **A**, which subsequently undergoes dehydration to afford the imine intermediate **B**. The XH group of intermediate **B** then performs a nucleophilic attack on the imine moiety, leading to the formation of intermediate **C**. Finally, intermediate **C** undergoes oxidative aromatization in the presence of atmospheric oxygen under the reaction conditions, yielding benzothiazole derivatives **137**.

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM. This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Scheme 37 Synthesis of thiazole using Ca@zeolite-Y/Fe_3O_4 supported 4-methylpyridinium ionic liquid.

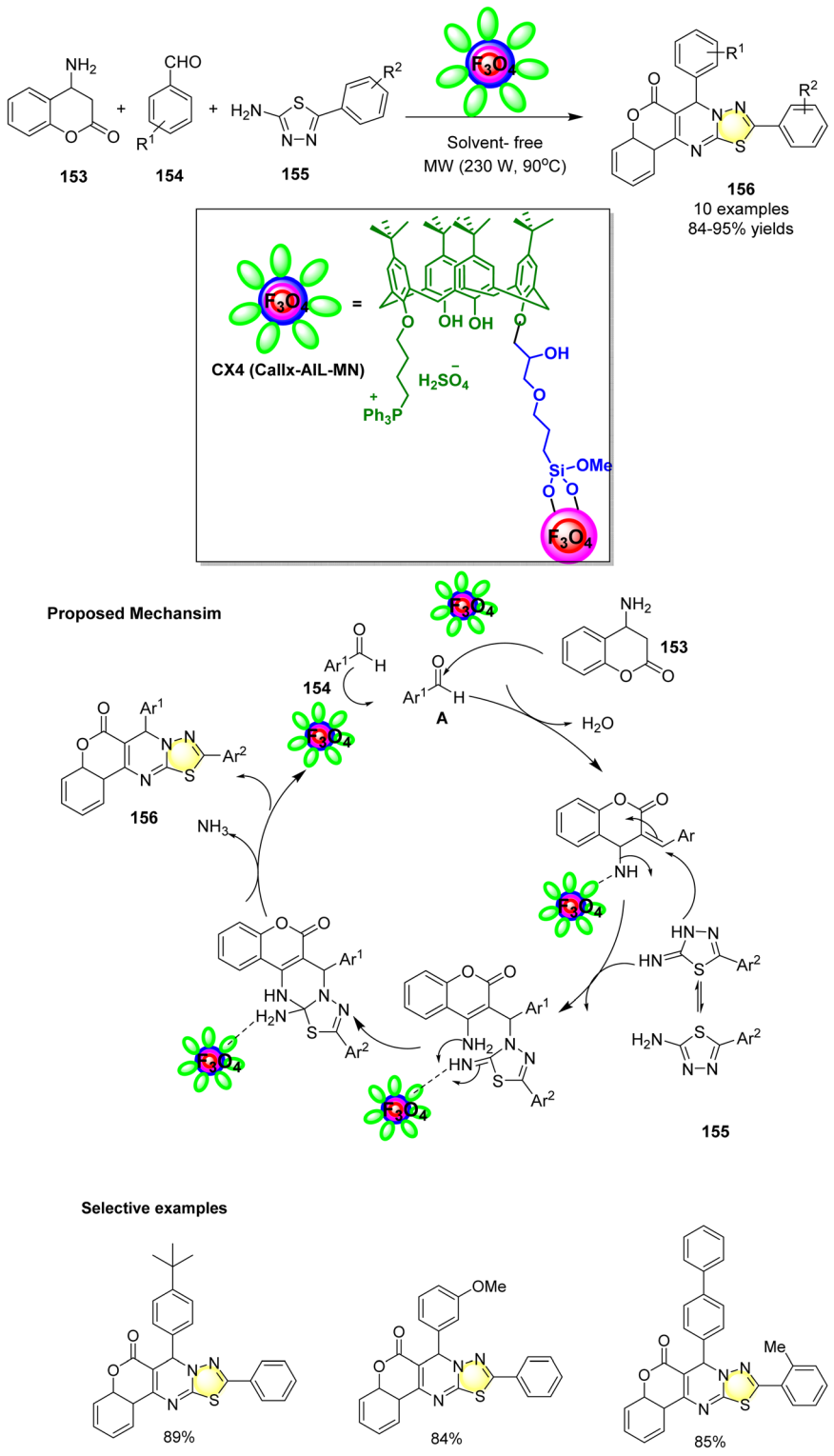
The integration of a Brønsted acidic ionic liquid with TEOS presents an innovative route to designing efficient heterogeneous catalytic systems, offering high product yields, straightforward product isolation, and insignificant migration of the ionic liquid into the organic phase.

In 2021, Rostami and co-authors[105] developed an innovative and resource-efficient synthetic strategy for accessing thiazole-2-imine derivatives **141**. This protocol involves the reaction between primary amines **138**, phenyl isothiocyanate **139**, and phenacyl bromide derivatives **140** in the presence of $COFe_2O_4$@SiO_2-PA-CC-Guanidine-SA as a magnetic nano-catalyst in high yields ranging from 88–97%. This nanocatalyst allows for easy recovery and multiple cycles of reuse (Scheme 34). The proposed mechanism for the synthesis of thiazole-2-imines from primary amines **138**, phenyl isothiocyanates **139**, and phenacyl bromide derivatives **140** is illustrated in Scheme 34.[106] Initially, nucleophilic addition of the primary amines **138** to phenyl isothiocyanate **139** affords intermediate **A**. The C=S group of intermediate **A** then attacks the C–Br bond of phenacyl bromide **140**, generating intermediate **B**. Subsequently, the PhNH group in intermediate **B** reacts with the carbonyl group activated by the acidic nanocatalyst to form intermediate **C**, which, upon dehydration, yields the desired thiazole-2-imine **141**. The nanocatalyst can be conveniently recovered from the reaction mixture and reused across multiple cycles. This method is favourable because of its mild conditions, ease of execution, and satisfactory to high yields. The catalyst showcased impressive stability, sustaining its performance over five repeated uses without notable deactivation.

In the year 2022, Mehdi Kalhor and Zohre Zarnegar[107] developed a novel, highly efficient, and multifunctional nanocatalyst, comprising Ni nanoparticles supported on zeolite-Y and functionalized with an imidazolium-based ionic liquid (Ni@zeolite-Im-IL), which was developed and thoroughly characterized. This hybrid catalyst was applied in a green synthetic protocol in the fabrication of 2-aminothiazoles and 2-arylbenzimidazoles. In particular, the catalyst showed excellent performance in the tandem reaction pathway for 2-aminothiazoles **144** through the condensation of ketones bearing a methyl group **142**, thiourea **143**, and iodine in DMSO at 80 °C, achieving yields ranging from 85% to 98%. Among its various advantages, this technique significantly lowers the required reaction time, high product purity, notable catalytic stability and activity, and efficient recyclability of the metal–supported ionic liquid nano-catalyst (Scheme 35).

In the year 2023, Kalhor and co-authors[108] described the development and fabrication of magnetically separable nanomaterial-based catalyst, Fe_3O_4@Zeolite-Y functionalized with *N*-methylimidazolium ionic liquid (1-MeIm IL@ZY-Fe_3O_4). The catalyst exhibited remarkable efficiency in the environmentally friendly, three-component synthesis of *N*-heterocyclic 1,3-thiazolidin-4-one derivatives **148** using aromatic aldehydes **145**, 2-aminobenzimidazoles (or 2-aminobenzothiazoles) **146**, and thioglycolic acid **147** in ethanol at room temperature (Scheme 36). Moreover, it demonstrated high yields (87–96%),

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

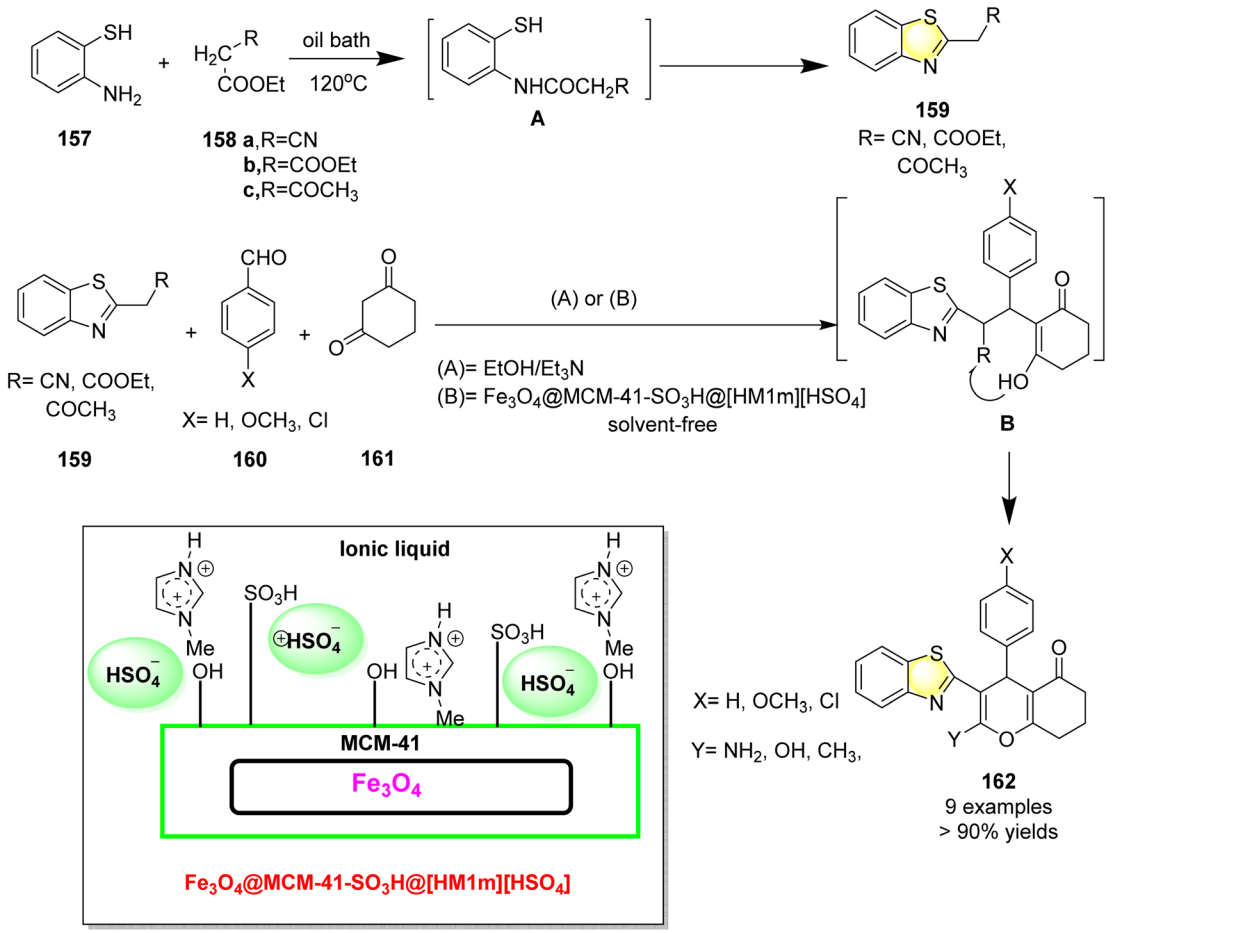


Scheme 38 Synthesis of thiazole using an acidic ionic liquid (Calix-AIL-MN).

rapid reaction times (15–21 min), and reusability over six cycles without loss of efficiency. At the onset of the catalytic reaction, 1-MeIm IL@ZY-Fe_3O_4 activates the aromatic aldehydes **145** carbonyl group through its organic functional sites and the Fe-based Lewis acid centres on the zeolite surface, generating intermediate **A**. The nucleophilic amine group of 2-amino-benzimidazoles (or 2-aminobenzothiazoles) **146** then attacks the activated aldehyde to form species **B**, which undergoes catalytic oxidation and dehydration to yield the Schiff base **C**. Subsequently, thioglycolic acid **147** (SH) performs

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



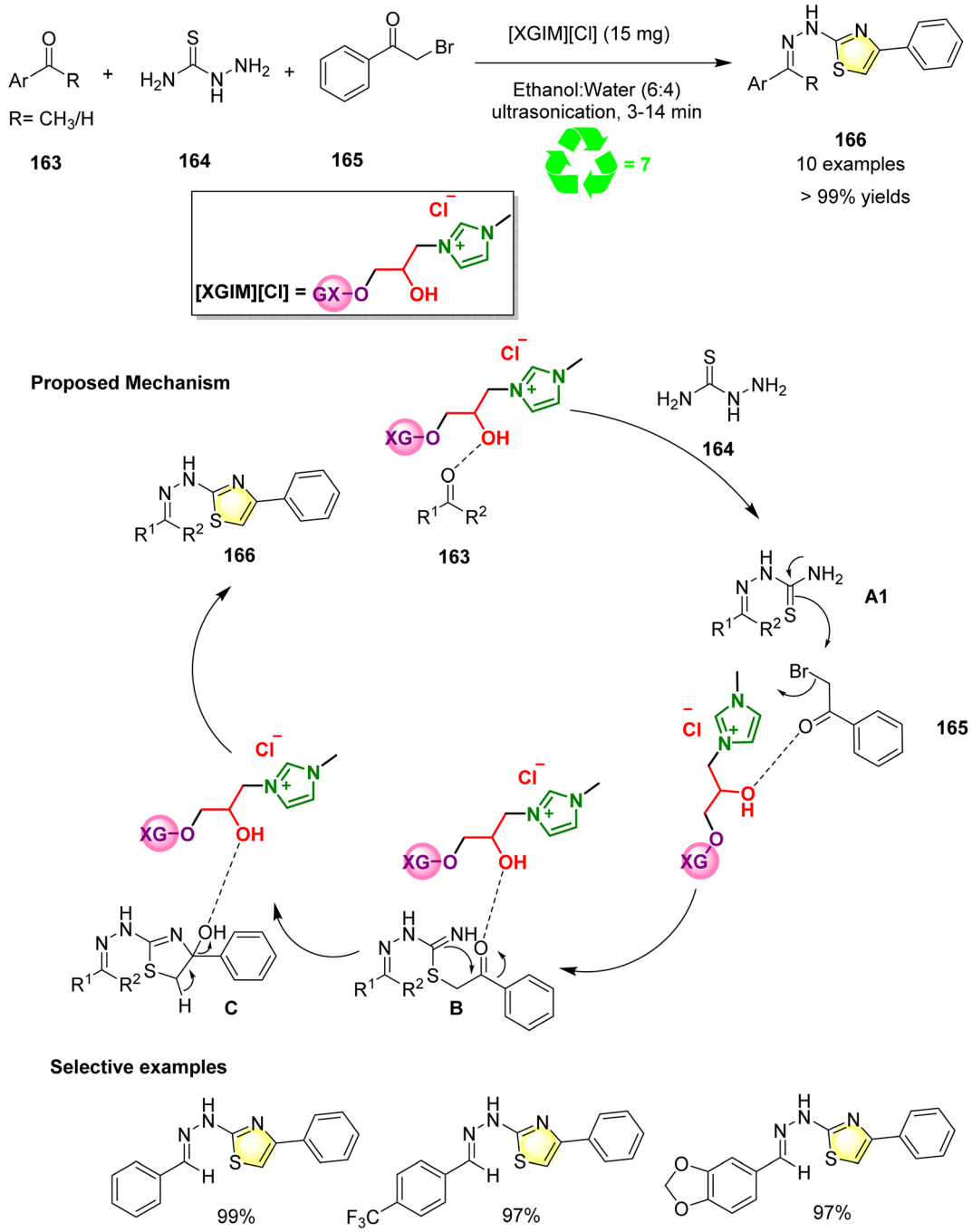
Scheme 39 Synthesis of thiazole using Fe_3O_4@MCM-41-SO_3H@[HMIm][HSO_4] as a magnetically recoverable ionic liquid-based nanocatalyst.

a nucleophilic attack, producing intermediate **D**. Finally, intramolecular cyclization accompanied by water elimination affords the *N*-heterocyclic 1,3-thiazolidin-4-one derivatives **148**. The study highlights the potential of this ionic-liquid-functionalized magnetic nano-catalyst for sustainable and efficient heterocyclic synthesis.

In 2023, Kalhor *et al.*[109] developed a magnetically separable, multifunctional nanocatalyst composed of Ca@zeolite-Y/Fe_3O_4 embedded with a 4-methylpyridinium-based ionic liquid was designed and utilized as an effective platform for the green synthesis of 2-aminothiazole derivatives. The catalyst was prepared by functionalizing zeolite-Y with calcium ions and 4-methylpyridinium chloride, followed by incorporating Fe_3O_4 nanoparticles. The synthesized nanocomposite was utilized in a one-pot reaction to produce 2-aminothiazole derivatives **152** using acetophenone **149**, thiourea **150**, and trichloroisocyanuric acid (TCCA), **151** as an environmentally benign halogenating agent (Scheme 37). The reaction demonstrated excellent efficiency under mild conditions (80 °C in ethanol), yielding products with high purity and good yields (75–92% yields). This technique ensures environmental compatibility by minimizing reliance on toxic iodine reagents and benefits from easy magnetic recovery, reusability, rapid reaction time, and operational simplicity. Overall, the study presents a sustainable and efficient strategy for the synthesis of biologically relevant thiazole derivatives, employing a recyclable heterogeneous nanocatalyst.

Subsequently, in 2024, Khalil *et al.*[110] constructed an innovative catalyst system by immobilizing a calixarene-derived acidic ionic liquid on Fe_3O_4 magnetic nanoparticles modified with epoxy-functionalized silica (Calix-AIL-MN), which proved effective for the synthesis of chromeno-thiadiazol pyrimidine derivatives **156**. This one-pot, three-component reaction involved amino-substituted coumarin derivative **153**, various aldehydes **154**, and amino-functionalized thiadiazole **155** under microwave irradiation (230 W, 90 °C), carried out without the use of solvent. The transformation concluded in 16 to 24 minutes, providing the target compounds in high yields, reaching up to 84–95%. The proposed mechanisms for the formation of chromeno-thiadiazol pyrimidine derivatives **156** under microwave conditions are illustrated in Scheme 38. Initially, the catalyst activates the aldehyde **154** to form intermediate **A**, which condenses with amino-substituted coumarin to give **B**. Under microwave irradiation, the tautomeric form undergoes Michael addition, cyclization, and ammonia elimination to yield chromeno-thiadiazol pyrimidine derivatives **156**.

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



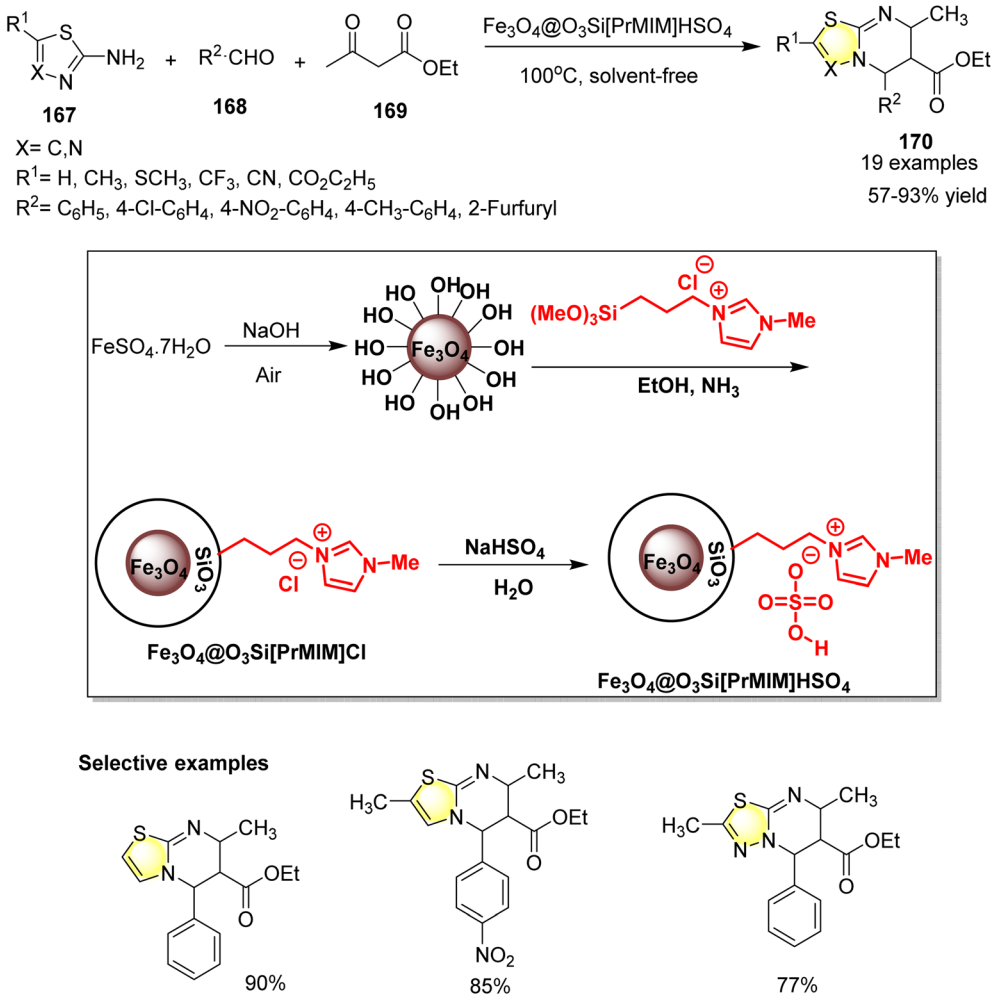
Scheme 40 Synthesis of thiazole using xanthan gum-supported ionic liquid [XGIM][Cl].

This method combines high efficiency, rapid reaction times, and eco-friendliness, making it a sustainable route for the synthesis of important heterocycles (Scheme 38).

In the same year, 2024, Mohareb *et al.*[111] introduced an innovative collection of heterocyclic scaffolds incorporating a benzothiazole moiety **162** through an efficient synthetic protocol *via* both conventional and ionic liquid-immobilized multi-component reactions from the reaction of 2-aminothiophenol **157** with substituted esters **158** to produce the desired product **159**. Furthermore, the desired product **159** underwent multi-component reaction with aldehydes **160** and cyclohexan-1,3-dione **161** using two different conditions, including first the use of solvent and regular catalyst, and secondly using Fe_3O_4@MCM-41-SO_3H@[HMIm][HSO_4] as a magnetically recoverable ionic liquid-based nanocatalyst under solvent-free conditions to afford 4*H*-chromen-5-(6*H*)-one derivatives **162** with good yields (>90% yields). This work highlights the dual benefit of green ionic liquid catalysis and medicinally

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Scheme 41 Synthesis of thiazole using Brønsted acidic ionic liquid Fe_3O_4@O_3Si [PrMIM]HSO_4.

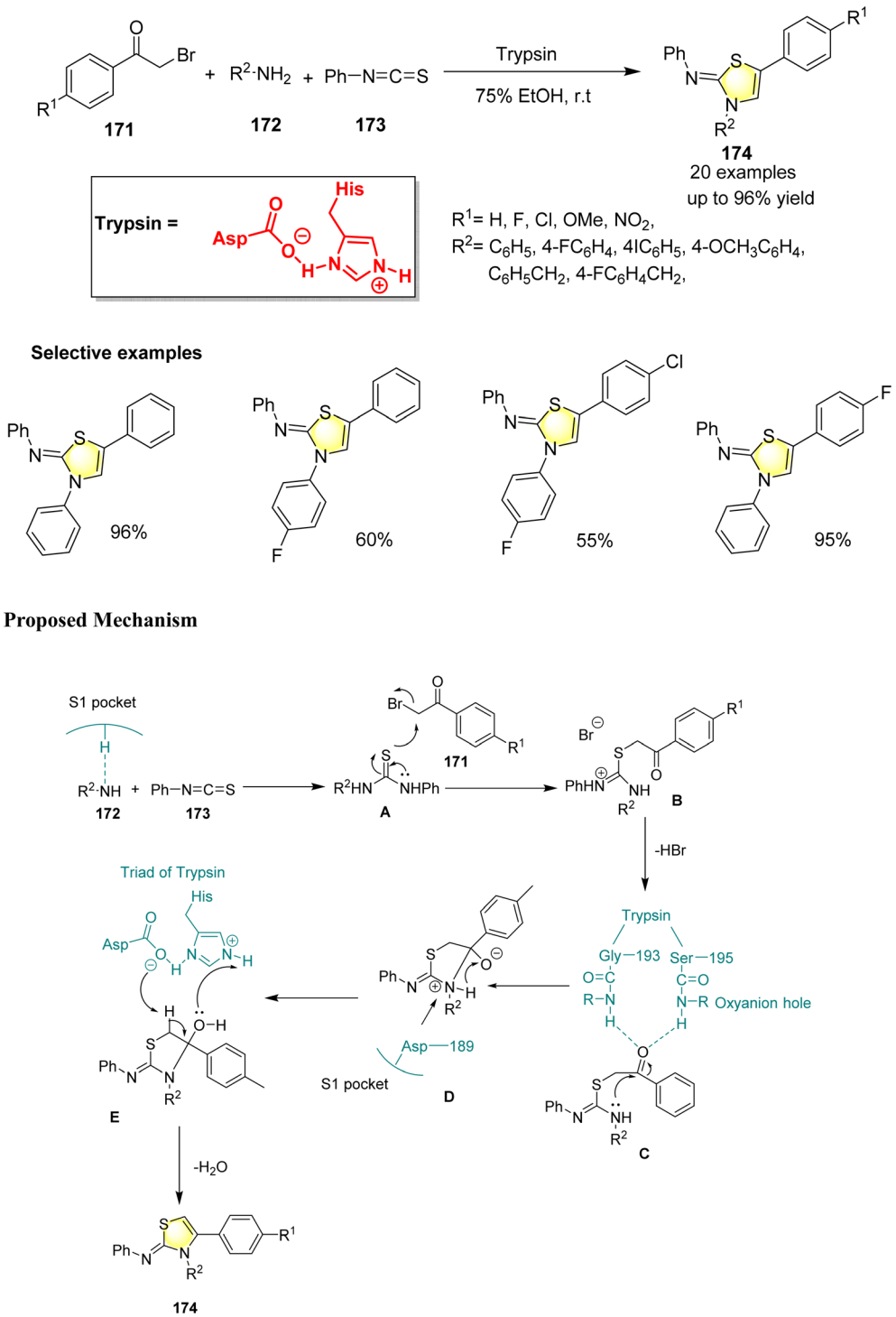
promising thiazole scaffolds, contributing to sustainable heterocyclic drug development (Scheme 39).

In 2025, Ayushi Aggarwal and Harish Kumar Chopra[112] reported a xanthan gum-supported ionic liquid catalyst, [XGIM][Cl], which was developed and implemented in an efficient multicomponent reaction to produce phenyl hydrazine-substituted thiazole derivatives **166**. The method utilized substituted aldehydes/ketones **163**, thiosemicarbazide **164**, and phenacyl bromide **165** under mild conditions, delivering excellent yields (up to >98%) within a short reaction time. As illustrated in the proposed mechanism (Scheme 40), substituted aldehydes/ketones **163** react with thiosemicarbazide **164** in the presence of [XGIM][Cl] to form imine intermediate **A**. The sulfur atom of **A** then attacks phenacyl bromide **165**, yielding intermediate **B**. Subsequent intramolecular cyclization between the imine NH and the activated carbonyl group produces intermediate **C**, which, upon dehydration, affords the phenyl hydrazine-substituted thiazole derivatives **166**. The [XGIM][Cl] catalyst enhances the electrophilicity of the carbonyl group, thereby facilitating the formation of intermediates **A** and **C**. Notably, the catalyst exhibited outstanding recyclability, maintaining its catalytic performance across seven successive cycles, thus underscoring its sustainability and green chemistry potential.

In the corresponding year, Le *et al.*[113] outlined a novel heterogeneous catalytic system in which a Brønsted acidic ionic liquid was immobilized on nano magnetite (Fe_3O_4) synthesized *via* oxidative precipitation. The resulting catalyst, Fe_3O_4@O_3Si [PrMIM]HSO_4, was successfully applied to a clean, one-pot reaction utilizing three reactants in the absence of solvent involving amino-functionalized thiazole scaffolds **167**, aldehydes bearing aromatic substituents **168**, along with ethyl acetoacetate **169**, yielding thiazolo-annulated pyrimidine derivatives **170** in excellent yields ranging from 57% to 93%. Notably, the catalyst maintained high stability and magnetic retrievability (98%) and was effectively reused for up to seven reaction cycles without significant loss of activity, with minimal loss of activity (Scheme 41). This work provides an efficient and recyclable nanocatalyst platform, advancing green chemistry approaches in heterocyclic synthesis.

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



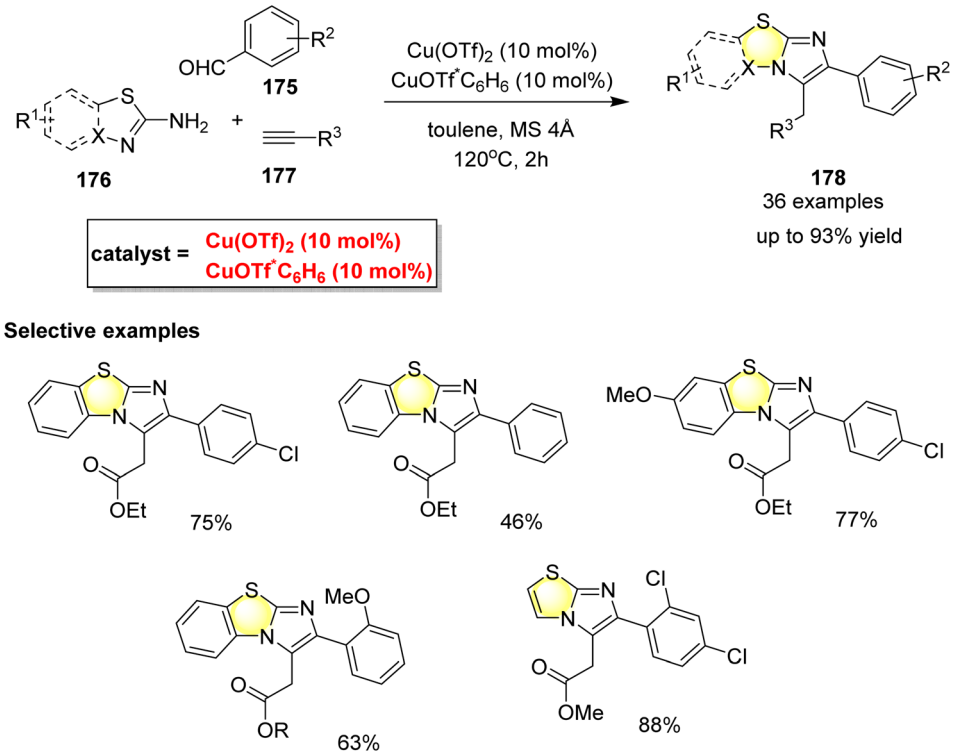
Scheme 42 Synthesis of thiazole derivatives catalyzed by trypsin from porcine pancreas.

4.4. Comparative insights: non-ionic liquid green strategies

Ionic liquids have gained recognition as a green medium in heterocyclic synthesis; however, various non-ionic liquid methods also offer significant ecological benefits.[114] These include enzyme catalysis, deep eutectic solvents (DESs), multi-component reactions facilitated by transition metal catalysts, and methods utilizing nano-catalysts.[115] Recently, Wang *et al.*[116] introduced a dual-atom Co/Ni catalytic system that enables selective C–O bond activation and *N*-functionalization of lignin-derived substrates, illustrating the growing promise of nano-structured catalysts in advancing sustainable chemical transformations. In this section, a curated overview of non-ionic liquid green methodologies for thiazole synthesis is

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Scheme 43 Synthesis of thiazole using copper(I,II) catalysis.

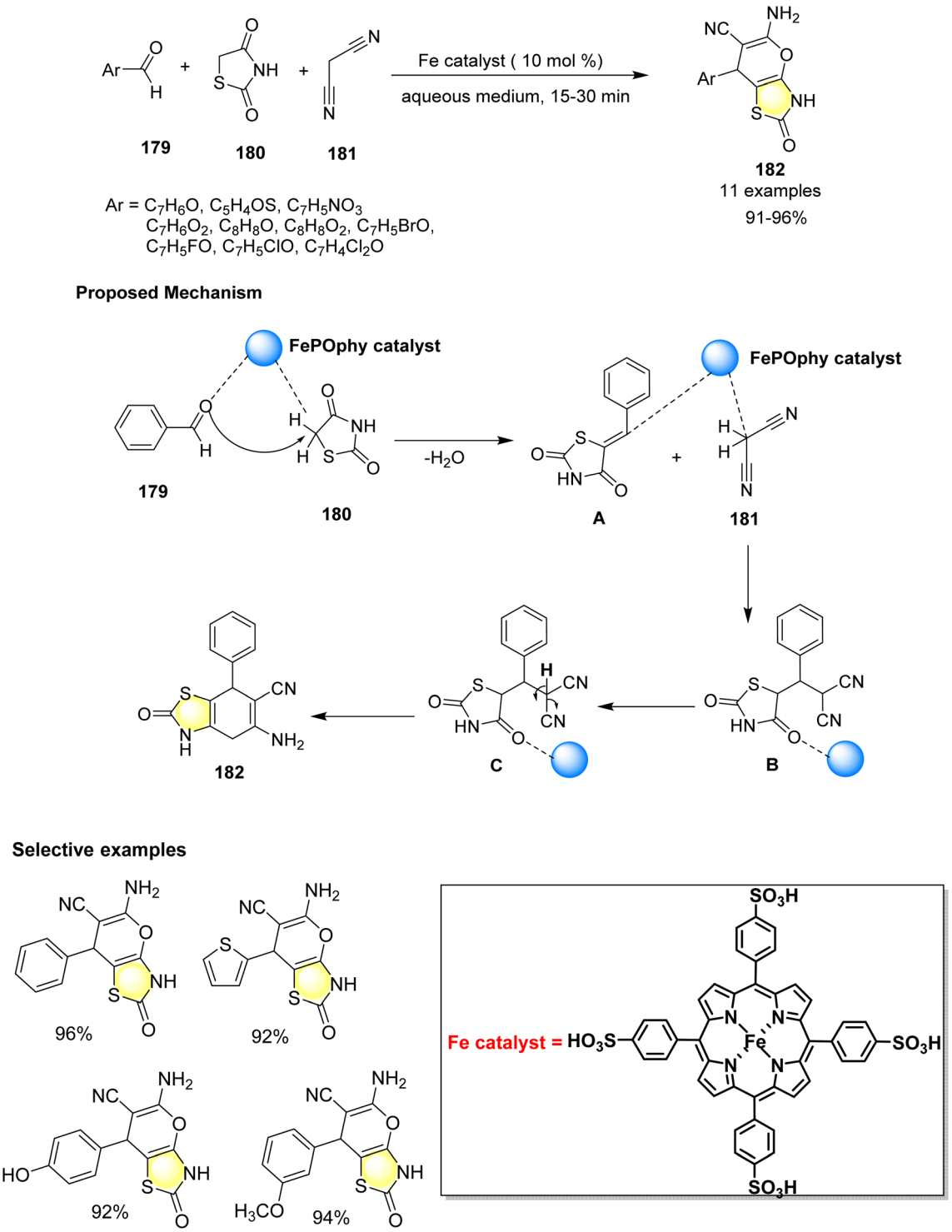
presented, providing a comparative perspective to evaluate the specific merits and limitations of ionic liquid-based systems.

In 2017, Zhou and co-authors[117] reported that a first Trypsin from porcine pancreas catalysed a novel one-pot three-component reaction of α-bromoketone **171**, primary alkylamines **172**, and phenyl isothiocyanate **173**, leading to the efficient synthesis of thiazole-imine compounds **174**. The transformations were carried out under ambient conditions in ethanol, delivering high product yields between 55% and 98%. The plausible mechanism for the 3CRs is depicted in Scheme 42. The primary alkylamines **172** react with phenyl isothiocyanate **173** in Trypsin's S1 pocket to form thiourea **A**, which undergoes nucleophilic alkylation with α-bromoketone **171** to give intermediates **B** and **C**. The cyclization of **C**, stabilized by the oxyanion hole and Asp-189, followed by deprotonation and dehydration *via* the His-57, Asp-102, Ser-195 triad, leads to the thiazole-imine compounds **174**. The study demonstrated the enzyme's broad substrate tolerance and high catalytic performance. This innovative strategy highlights the potential of enzyme-catalyzed multicomponent reactions as sustainable methods for assembling thiazol-2-imine derivatives, thus expanding the functional scope of biocatalysts in green organic synthesis.

In the same year, Rassokhina and co-authors[118] developed a straightforward procedure for generating imidazo-fused thiazoles with structural modifications **178** using substituted benzaldehyde derivatives **175**, aminothiazole derivatives **176**, and acetylenic compounds **177** as starting materials mediated by copper in its +1/+2 oxidation state. This strategy facilitated the efficient construction of a broad range of imidazo-fused benzothiazoles with aryl substituents, imidazo-fused thiazole derivatives, and thiadiazolo-imidazole fused systems (Scheme 43). The reactions proceeded smoothly, affording moderate to excellent yields of the target compounds, with some reaching up to 93%. Additionally, utilizing a continuous-flow system led to superior yields, with conversions approaching quantitative levels.

In 2024, Alzahrani and co-authors[119] developed an eco-friendly and efficient protocol, using an iron(III)-porphyrin (FePOphy) complex as a sustainable catalyst used in the formation of pyrano-fused thiazole carbonitrile compounds **182**. This protocol employs a single-pot, three-component condensation reaction using aromatic ring-based aldehydes **179**, 2,4-thiazolidinedione **180**, and malononitrile **181**, conducted at 60 °C under ambient air with magnetic stirring. An ethanol–water mixture served as the green solvent platform for conducting the reactions (H_2O/EtOH), yielding the target compounds in excellent yields ranging from 91% to 96%. As illustrated in Scheme 44, the proposed mechanism for the FePOphy-catalyzed synthesis of pyrano-fused thiazole carbonitrile compounds **182** under mild conditions proceeds through several steps. First, the FePOphy catalyst protonates the aromatic ring-based aldehydes **179**, enhancing their electrophilicity. The activated aldehyde then undergoes a Knoevenagel condensation with 2,4-thiazolidinedione **180** to form intermediate **A**. Subsequently, the CH_2 group of malononitrile **181** attacks the C=C bond, generating intermediate **B**. Finally, intramolecular cyclization through the reaction of the cyano

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Scheme 44 Development of thiazoles using FePOphy complexes as robust and recoverable catalysts.

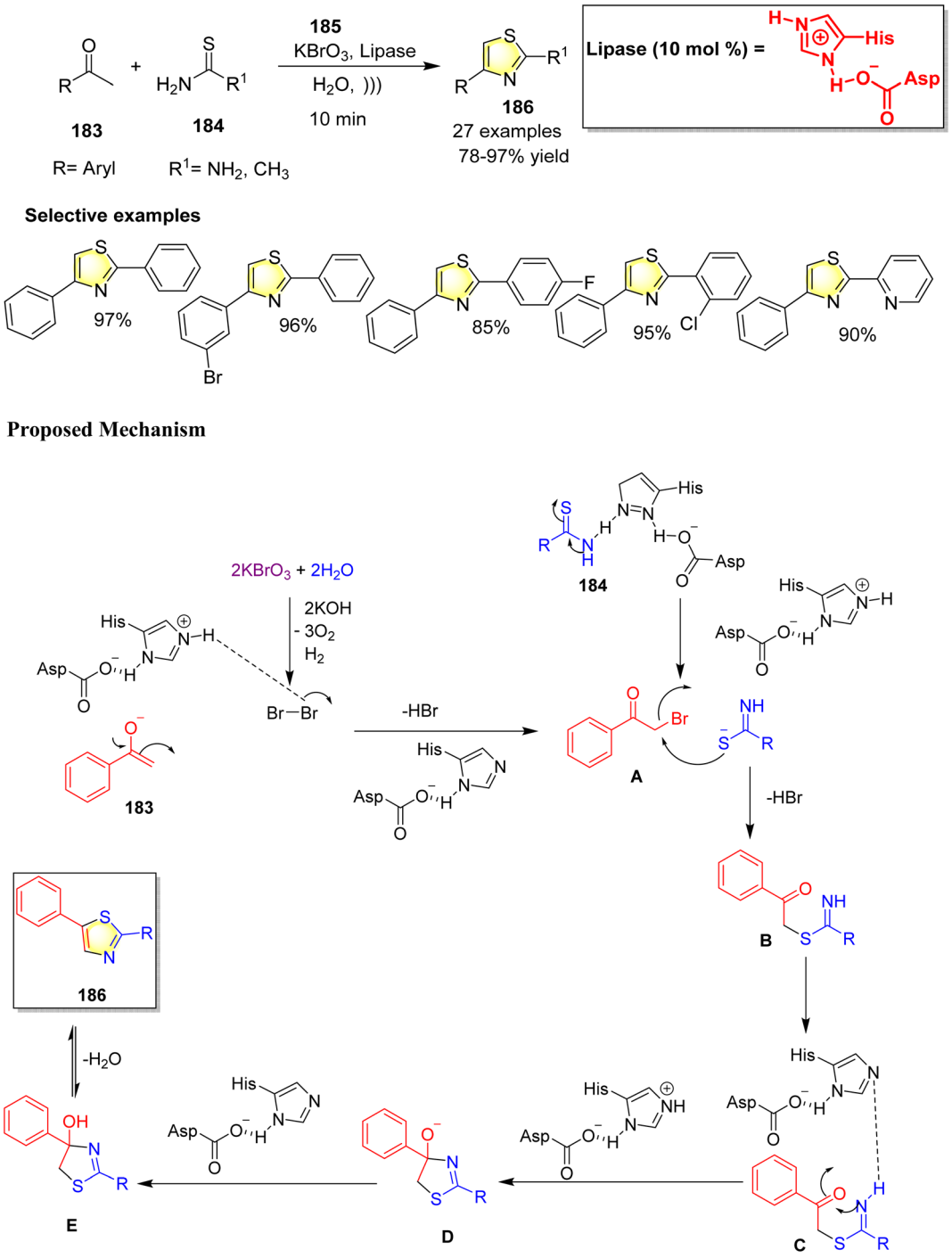
and hydroxyl groups produces the pyrano-fused thiazole carbonitrile derivatives.[120]

This sustainable approach benefits from mild conditions, high selectivity, minimal environmental impact, and the recyclability of the catalyst, making it a promising strategy in line with green chemistry objectives.

Subsequently, in 2024, Priya Mahaur and co-authors[121] introduced an innovative and efficient strategy for synthesizing 2,4-disubstituted thiazole **186**, compounds recognized for their wide-ranging biological and medicinal significance, by utilizing lipase serving as a sustainable biocatalyst with excellent selectivity. The condensation of aryl ethenone **183**, thioamide **184**,

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

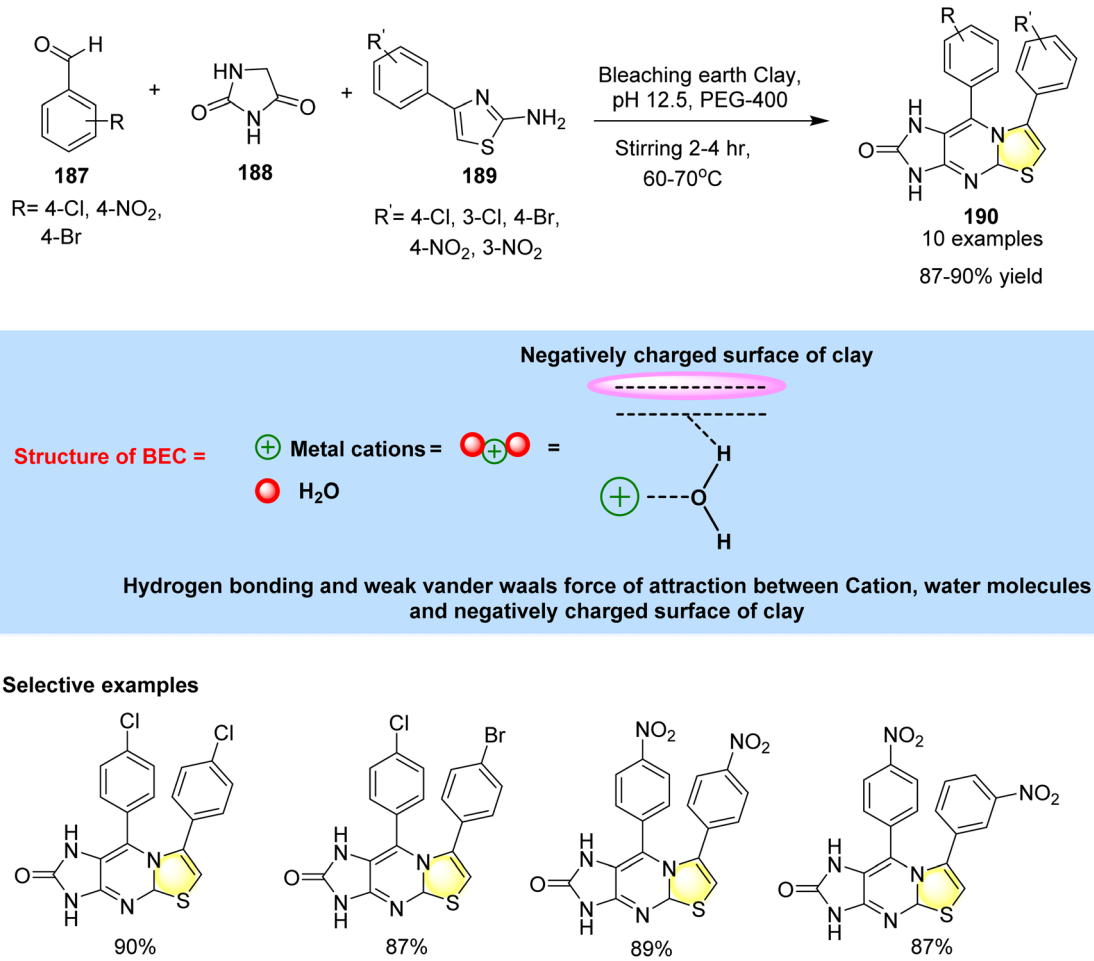


Scheme 45 Synthesis of thiazole using enzyme catalysis by lipase.

and $KBrO_3$ **185** is facilitated through ultrasonic energy under mild reaction conditions.

The proposed mechanism begins with enolization of aryl ethenone **183** under basic conditions to form intermediate **A**, which is converted to **B** in the presence of $KBrO_3$ **185** and aqueous media. Intermediate **B** then undergoes intermolecular nucleophilic attack by the enolized form of thioamide **184** to yield **C**. Subsequent intramolecular nucleophilic addition forms **D**, which undergoes dehydration in the presence of lipase to afford the 2,4-disubstituted thiazole **186** (Scheme 45). Furthermore, the application of ultrasound irradiation effectively accelerates the reaction, resulting in reduced reaction times and enhanced product yields ranging from 78% to 97%. The combination of lipase catalysis and ultrasound irradiation offers a green and sustainable strategy for producing these pharmacologically important thiazole derivatives. This method not only minimizes environmental impact but also holds promising applications in drug discovery and development.

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Scheme 46 Synthesis of thiazole using base catalyst, bleaching earth clay (BEC).

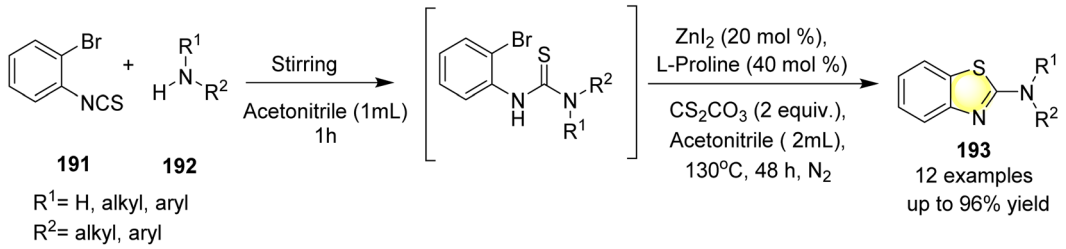
This strategy contributes to the advancement of thiazole synthesis by fostering more efficient and environmentally responsible chemical methodologies.

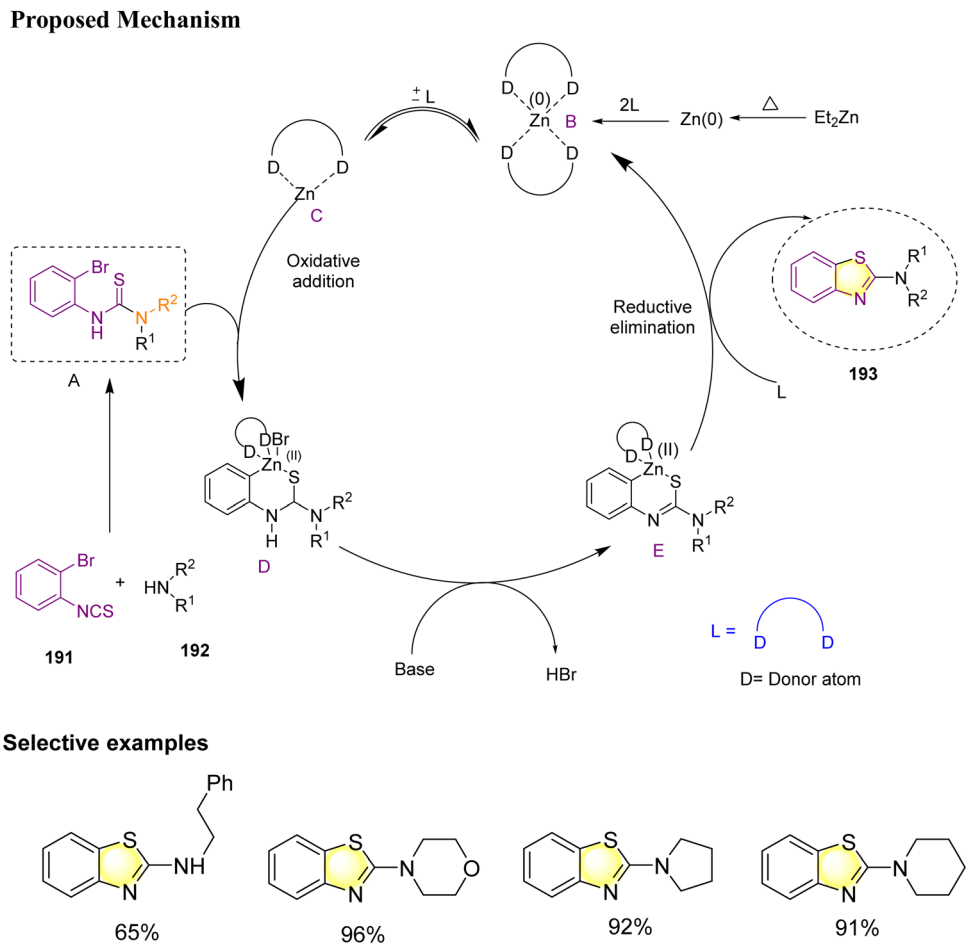
Again, in the same year, Mogle *et al.*[122] proposed a resource-efficient and streamlined method in pursuit of synthesizing thiazolo-annulated purine-2-one analogues **190** through a multicomponent reaction strategy that integrates purine and thiazole motifs. The process applies bleaching earth clay (BEC, pH 12.5) as a reusable solid base catalyst with polyethylene glycol-400 employed as an environmentally benign reaction medium, operating under mild conditions. The one-pot protocol couples substituted aromatic aldehydes **187**, hydantoin 188, and substituted 2-aminothiazoles **189**, affording a library of target compounds (**190a–j**) in high yields (>90%) along with reduced reaction durations (Scheme 46). Antibacterial evaluation revealed that several derivatives (notably **190a**, **190b**, **190d**, **190g**, and **190h**) exhibited significant activity against *Staphylococcus aureus* and *Escherichia coli*. This research underscores the significance of bleaching earth clay (BEC) employed as a sustainable and recyclable catalytic agent, promoting the sustainable synthesis of heterocyclic drug candidates by merging two bioactive structural frameworks with high pharmacological relevance.

In the year 2025, Neetha *et al.*[123] developed a new and practical synthetic strategy for producing 2-aminobenzo[*d*]thiazole derivatives **193**, employing a one-pot strategy that reacts 2-bromophenyl isothiocyanate **191** with various amines **192**. The reaction is catalyzed by a combination of diethylzinc (Et_2Zn) and DABCO, using Cs_2CO_3 in acetonitrile under a nitrogen atmosphere at 130 °C. The optimized protocol produces the desired compounds in moderate to excellent yields, with outcomes varying depending on the type of nitrogen-containing reactant employed. Based on prior knowledge of zinc catalysis, a plausible mechanism is proposed in Scheme 47. The amine **192** attacks 2-bromophenyl isothiocyanate **191** to form thiourea intermediate **A**. Thermal decomposition of Et_2Zn generates Zn(0), which, in the presence of DABCO, forms a complex **B** in equilibrium with **C**. The oxidative addition of the thiourea **A** to Zn(0) yields Zn(II) complex **D**, which undergoes cyclization and HBr elimination to form intermediate **E**. Finally, reductive elimination produces the 2-aminobenzo[*d*]thiazole derivatives **193**, regenerating Zn(0) complex **B** for further catalytic cycles.

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



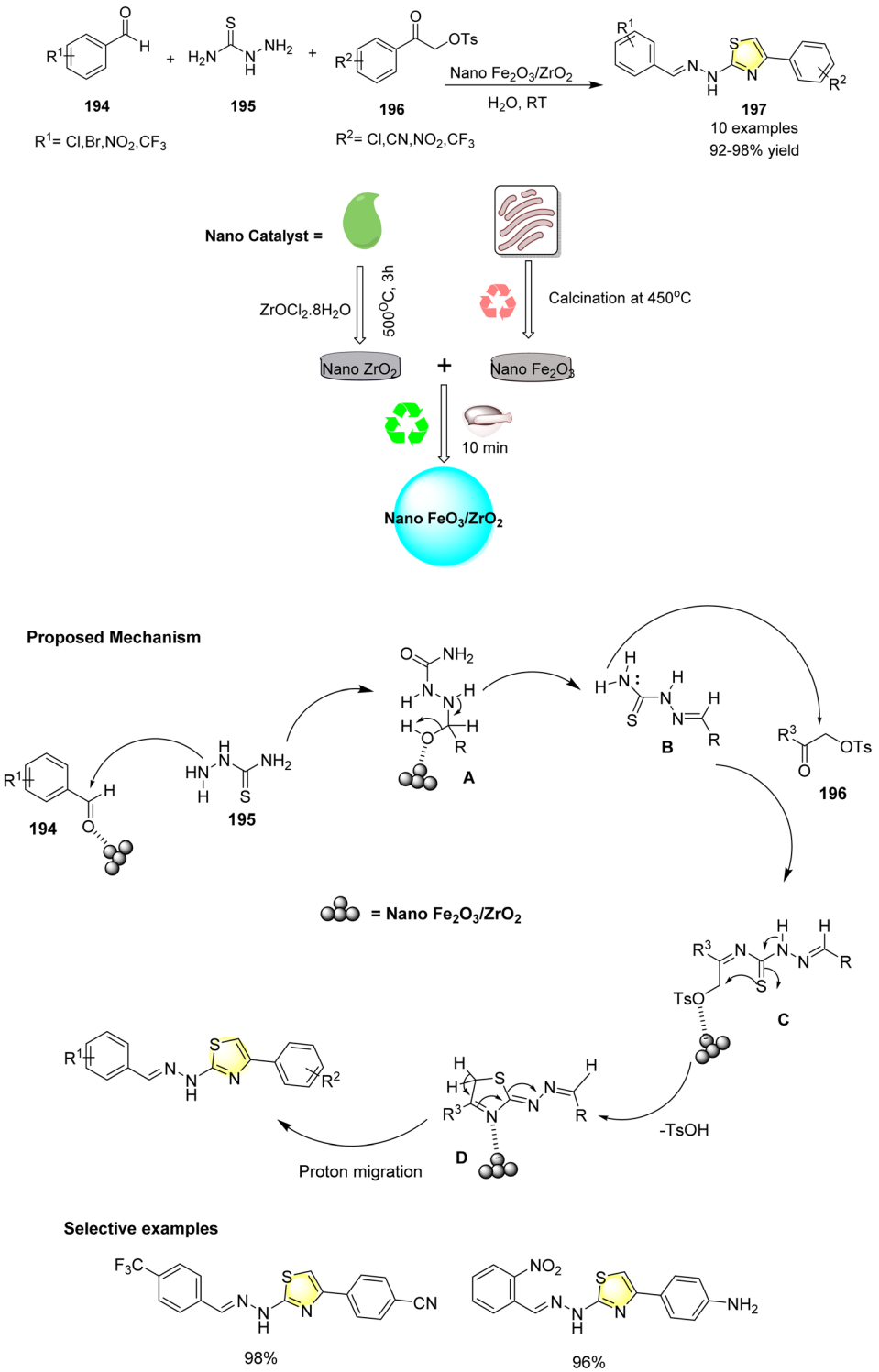


Scheme 47 Formation of thiazole using zinc(II)-catalysis.

The protocol exhibits broad substrate scope, efficiently accommodating aromatic, aliphatic, and cyclic secondary amines, with the latter demonstrating notably enhanced reactivity (up to 96% yield). A plausible mechanism involving Zn(0)/Zn(II) redox cycling and thiourea intermediates is proposed. This method offers a valuable, metal-catalysed, and scalable route to biologically important 2-aminobenzothiazole scaffolds, advancing the field of heterocyclic synthesis.

In 2025, Gurav and co-authors[124] developed a sustainable and retrievable Fe_2O_3/ZrO_2 nano-catalytic system obtained from iron oxide deposits and the extract of Ficus benghalensis leaves. A sustainable catalytic approach facilitated the rapid synthesis of novel hydrazinyl thiazole analogues **197** through a single-pot procedure of aromatic carbonyl compounds **194**, sulfur-containing hydrazine derivative **195**, along with phenyl group-

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



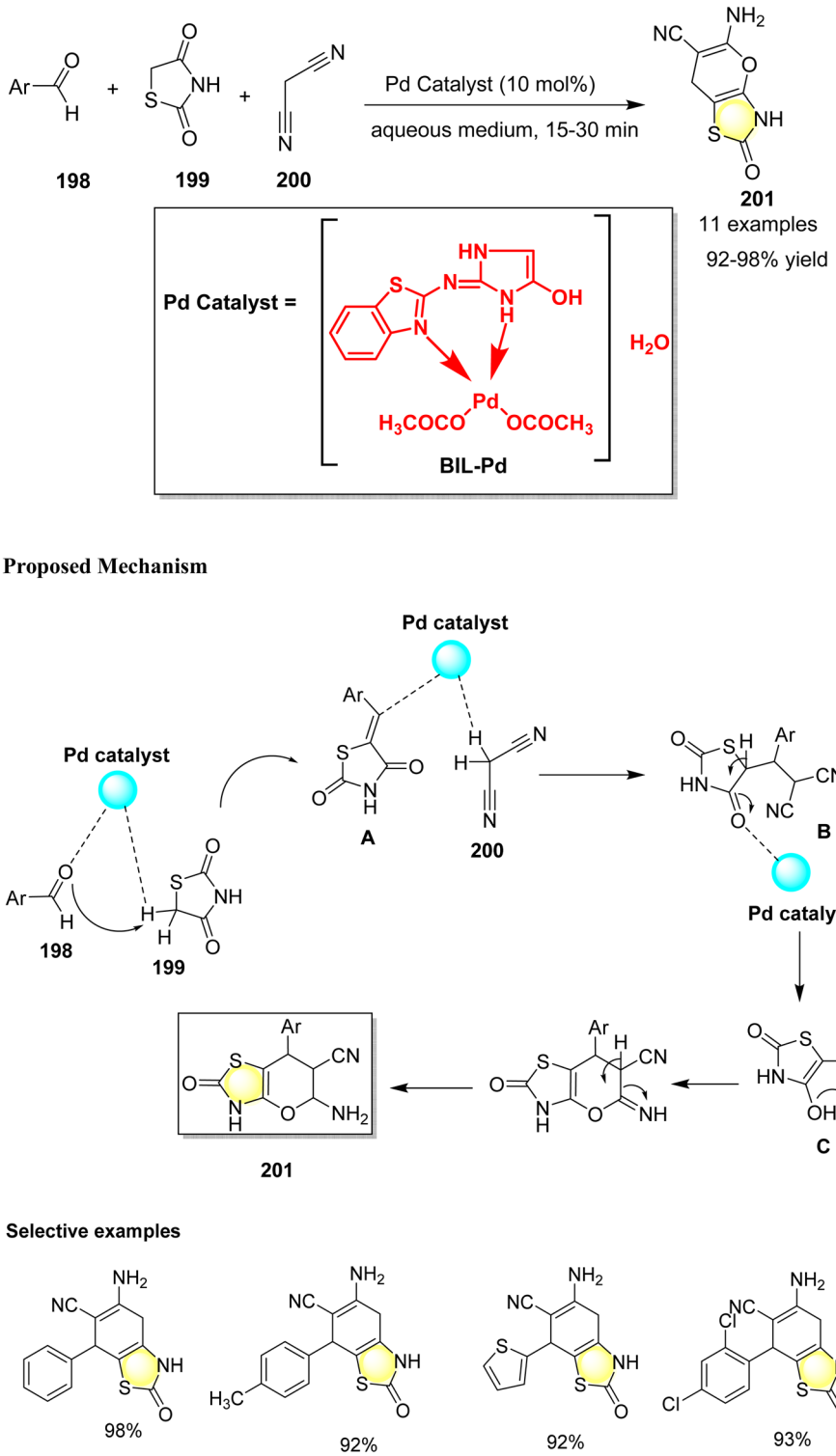
Scheme 48 Development of thiazole using rust-derived Fe_2O_3/ZrO_2 NPs catalysis.

containing acyl tosylate **196,** yielding the compounds produced with satisfactory to excellent yields (>98%).

The proposed reaction mechanism begins with the adsorption of the aromatic carbonyl compounds **194** onto the Fe_2O_3/ZrO_2 nanoparticle surface in aqueous medium, where the carbonyl carbon undergoes nucleophilic attack by the $-NH_2$ group of sulfur-containing hydrazine derivative **195,** to form intermediate **A,** followed by dehydration to afford the thiosemicarbazone intermediate **B.** An S_N2 attack of intermediate **B** on phenyl group-containing acyl tosylate **196** forms

© 2025 The Author(s). Published by the Royal Society of Chemistry

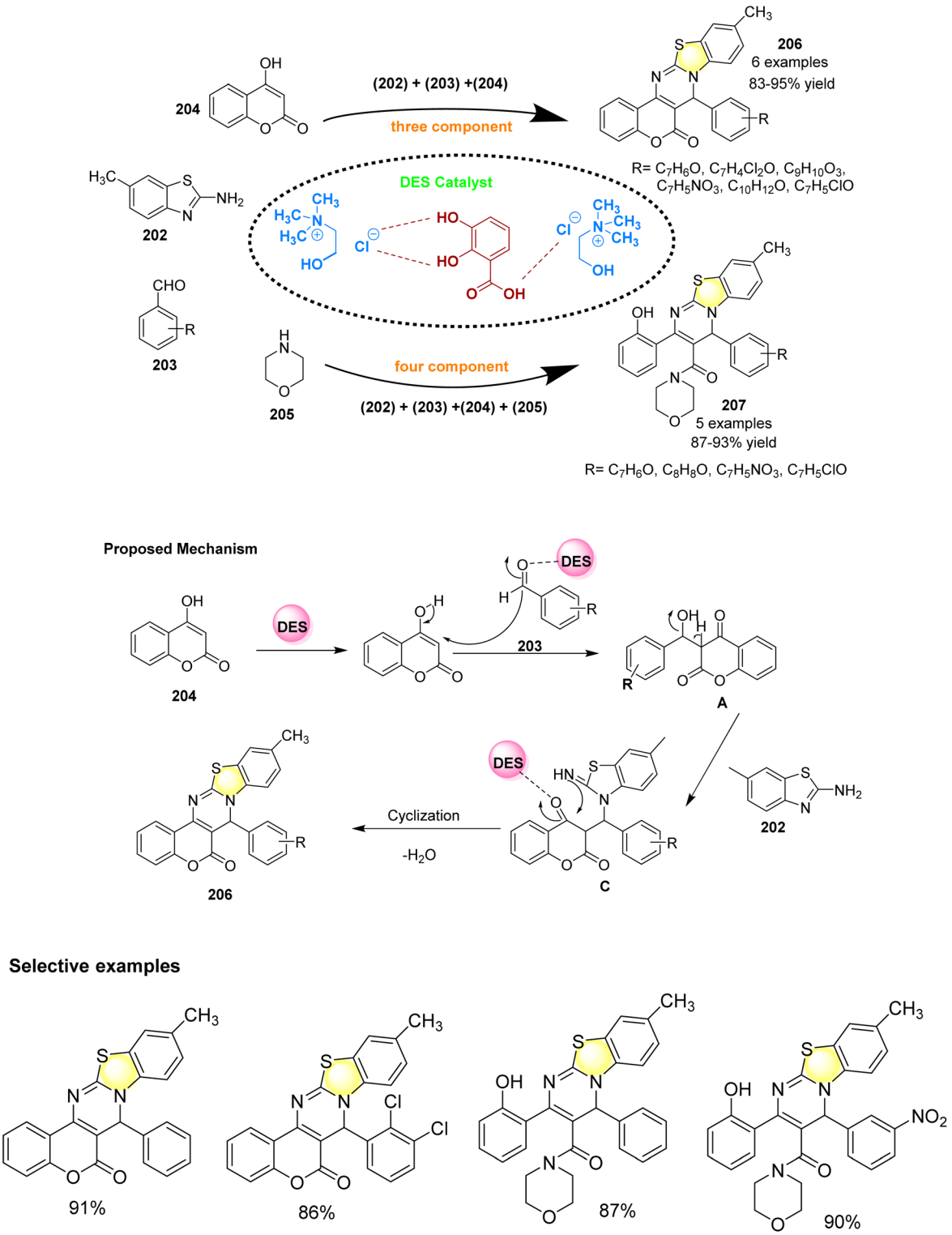
Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Scheme 49 Synthesis of thiazole using (BIL-Pd) complex.

intermediate **C**, which subsequently undergoes an SNi substitution to generate intermediate **D**. Finally, the proton migration then affords the novel hydrazinyl thiazole analogues **197** (Scheme 48). Among the synthesized compounds, **197c** exhibited notable anti-diabetic potential, showing significant inhibitory activity at low concentration levels, and compound **197b** showed the strongest antioxidant activity, demonstrating significant radical scavenging efficiency in DPPH examination. This study underscores the efficiency of Fe_2O_3/ZrO_2 nanoparticles sourced from rust as an eco-friendly and recyclable catalyst for the synthesis of biologically active thiazoles,

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



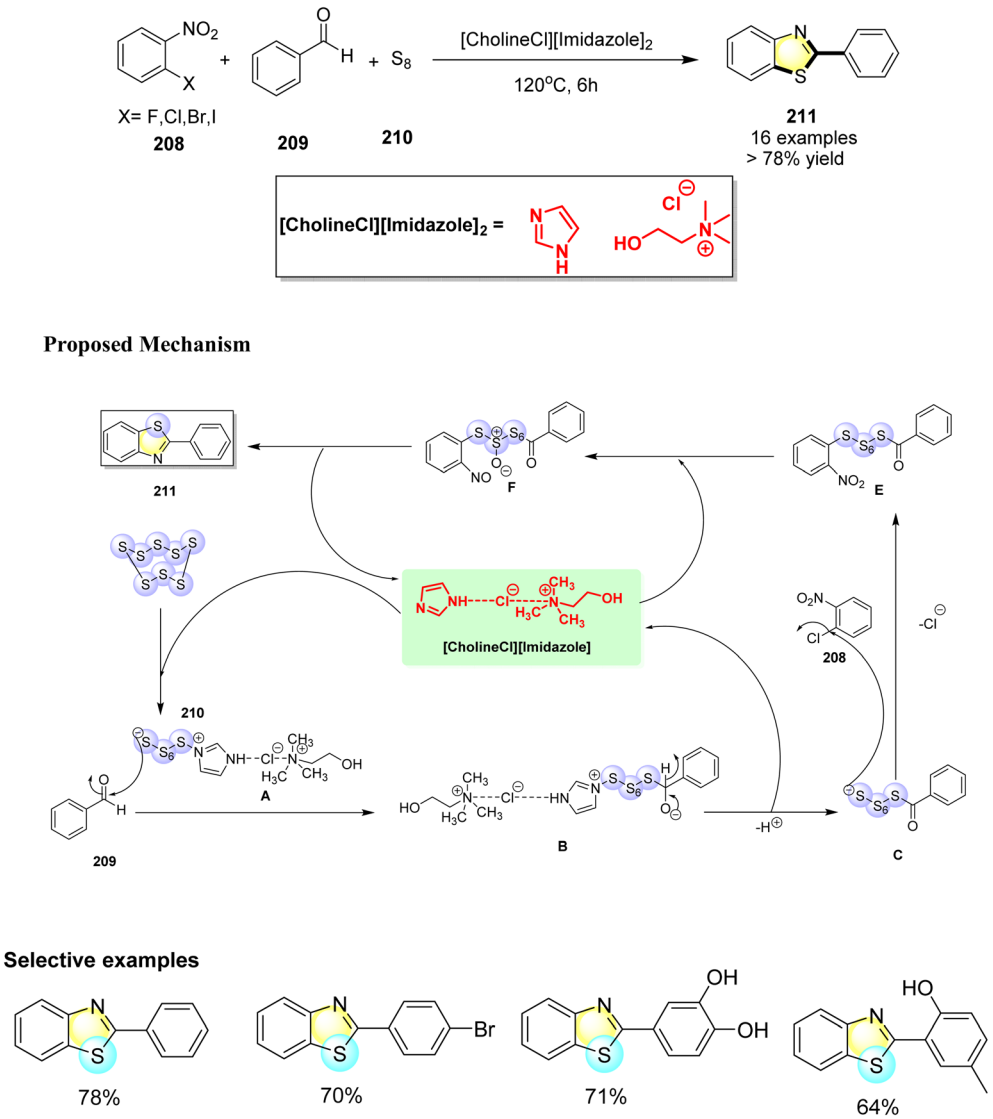
Scheme 50 Thiazole synthesis employing novel ChCl/HGA-based deep eutectic solvent.

contributing to sustainable approaches in pharmaceutical manufacturing.

In 2023, El-Remaily and co-workers[125] developed a novel set of metal complexes incorporating an imidazole-based heterocycle containing benzothiazol-2-ylimino functionality (BIL) ligands with palladium, iron, and nickel metal ions, which were synthesized and evaluated. Among these, the palladium-based complex (BIL-Pd) exhibited outstanding catalytic activity in promoting a green, one-pot multicomponent reaction involving aromatic aldehydes **198**, 2,4-thiazolidinedione **199**, and

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

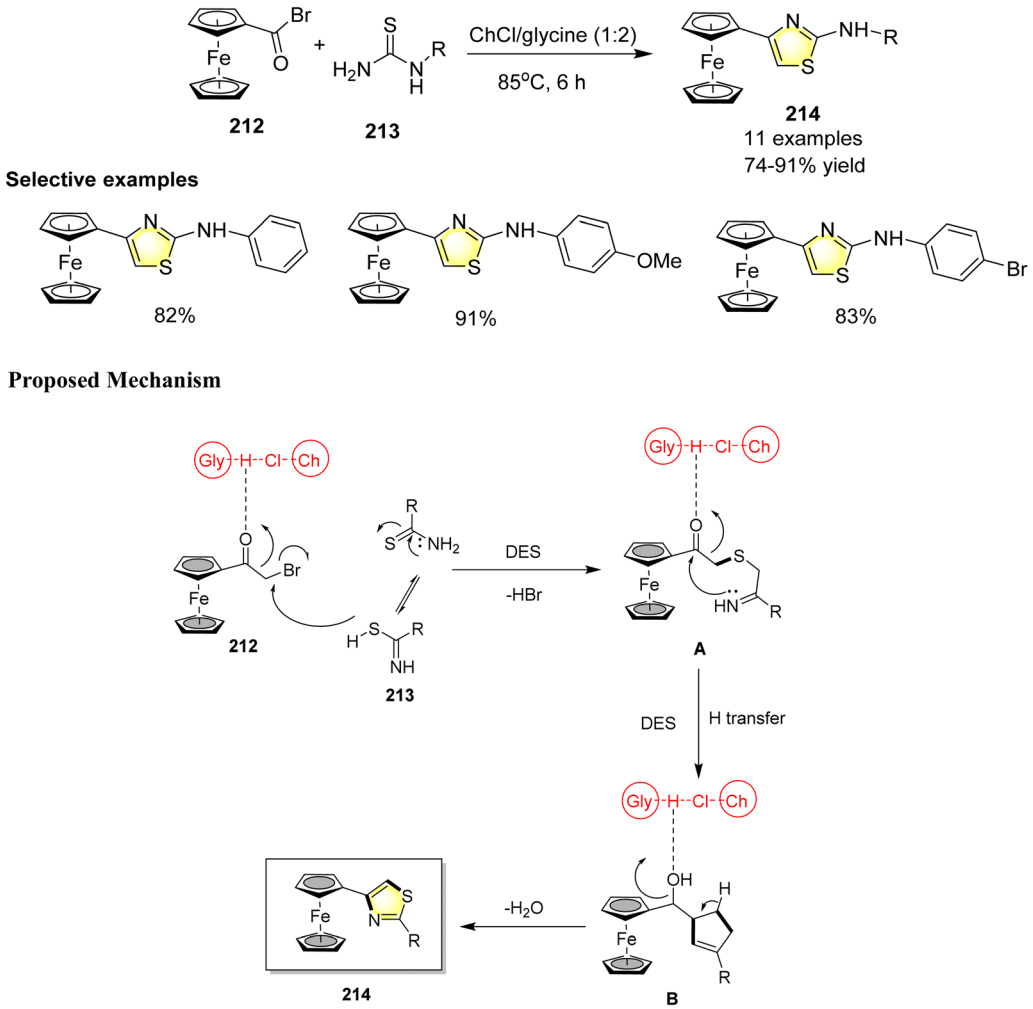


Scheme 51 Green synthesis of thiazole using choline chloride–imidazole-based DES.

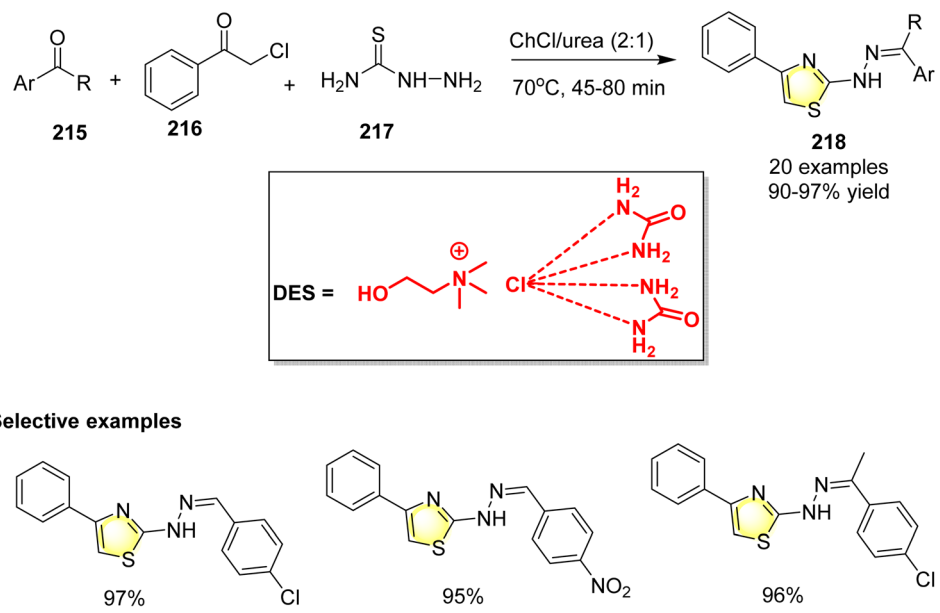
malononitrile **200**. This led to the efficient formation of thiazole-fused pyran ring systems bearing amino and nitrile functionalities **201**, subjected to environmentally responsible and standardized parameters (Scheme 49). The BIL-Pd complex functioned as a robust and reusable heterogeneous catalyst, delivering superior results compared to conventional Lewis's acids, base catalysts, and ionic liquids in terms of product yield and reaction efficiency. The catalyst exhibited high efficiency (up to 98% yield), reusability for six cycles, and favourable properties confirmed by DFT calculations. The activation of substrates by the BIL-Pd(II) catalyst involves synergistic hydrogen bonding and electrostatic interactions, as supported by spectroscopic and DFT studies. Through protonation of the carbonyl group, BIL-Pd effectively activates the carbonyl moiety of the aromatic aldehyde **198**, rendering it a suitable electrophile. The activated aldehyde then reacts with 2,4-thiazolidinedione **199** to yield the Knoevenagel intermediate **A**. Subsequent nucleophilic attack by the malononitrile methylene group generates intermediate **B**, which undergoes intramolecular cyclization to form intermediate **C**. Finally, conjugation-assisted ring closure leads to the formation of thiazole-fused pyran ring systems bearing amino and nitrile functionalities **201**.[120] The IR spectra showing red-shifts of ν(N–H) and ν(C=N) bands, along with the appearance of M–N and M–O vibrations, confirm metal coordination and charge redistribution, followed by ^{1}H NMR shifts also suggest hydrogen-bond formation. The DFT calculations reveal a reduced HOMO–LUMO energy gap and increased electrophilicity and electronegativity for the BIL-Pd complex, signifying enhanced charge transfer and catalytic activity. This work highlights BIL-Pd as a robust, recyclable, and eco-friendly catalyst for sustainable heterocyclic synthesis.

In 2025, Chen and co-authors[126] described the creation and use of a new deep eutectic solvent (DES), ChCl/HGA-DES, made from choline chloride and 2,3-dihydroxybenzoic acid (hypo gallic acid) in a 2 : 1 molar ratio. This DES was subsequently

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



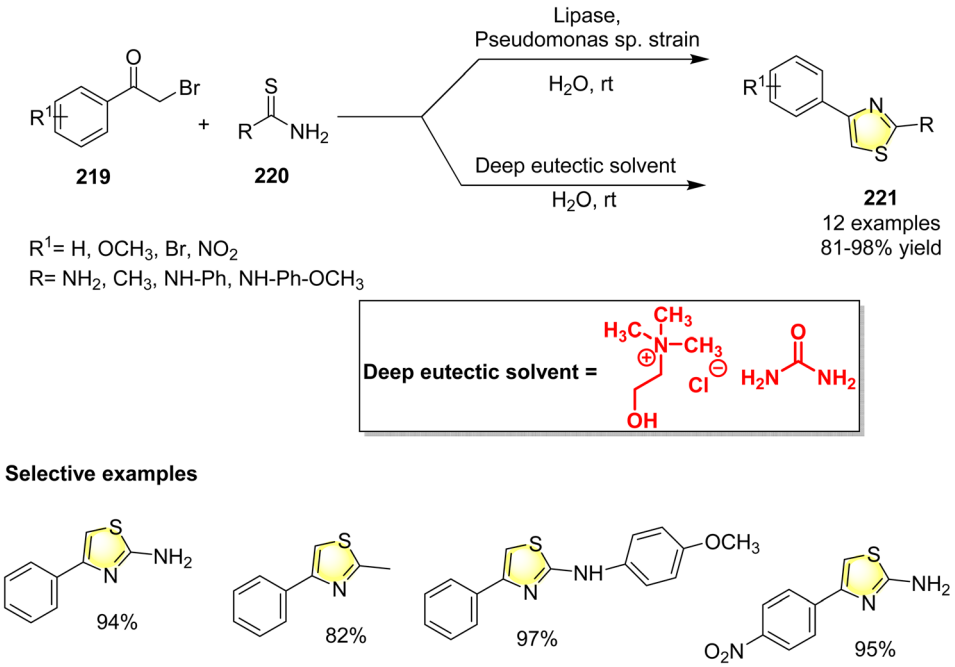
Scheme 52 Green synthesis of thiazoles using ChCl–glycerol DES.



Scheme 53 ChCl–urea deep eutectic solvent as a sustainable medium for thiazole formation.

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Scheme 54 Synthesis of thiazole using biocatalytic and deep eutectic solvent (DES).

employed, acting as an effective and repeatedly usable catalyst in the solvent-less formation of two novel classes of fused heterocyclic compounds: (i) chromeno-fused thiazolo pyrimidinone scaffolds **206a–f**, (ii) their morpholino-substituted methanone derivatives **207a–e** *via* a single-step condensation approach between 2-amino-6-methylbenzothiazole **202**, aldehyde **203**, 4-hydroxycoumarin **204**, and morpholine **205**. The reactions took place under mild conditions (70 °C), with high atom economy and excellent yields (up to 95%).

The proposed mechanism for the synthesis of **206a–f** is illustrated in Scheme 50. Initially, the DES catalyst activates the aldehyde **203**, forming intermediate **A** *via* dehydration. Condensation of **A** with 2-amino-6-methyl-benzothiazole **202** produces intermediate **B**, which undergoes intramolecular cyclization and water elimination to yield the final products chromeno-fused thiazolo pyrimidinone scaffolds **206a–f.**[127] Furthermore, an additional step is involved as compared to **206a–f**, including nucleophilic attack by morpholine and coumarin ring opening to produce morpholino-substituted methanone derivatives **207a–e**. DES catalyst showed good recyclability over four cycles with minimal activity loss. This work emphasizes the versatile catalytic functionality of DESs serving both as solvent and catalyst, providing a sustainable alternative to traditional reagents in heterocyclic synthesis.

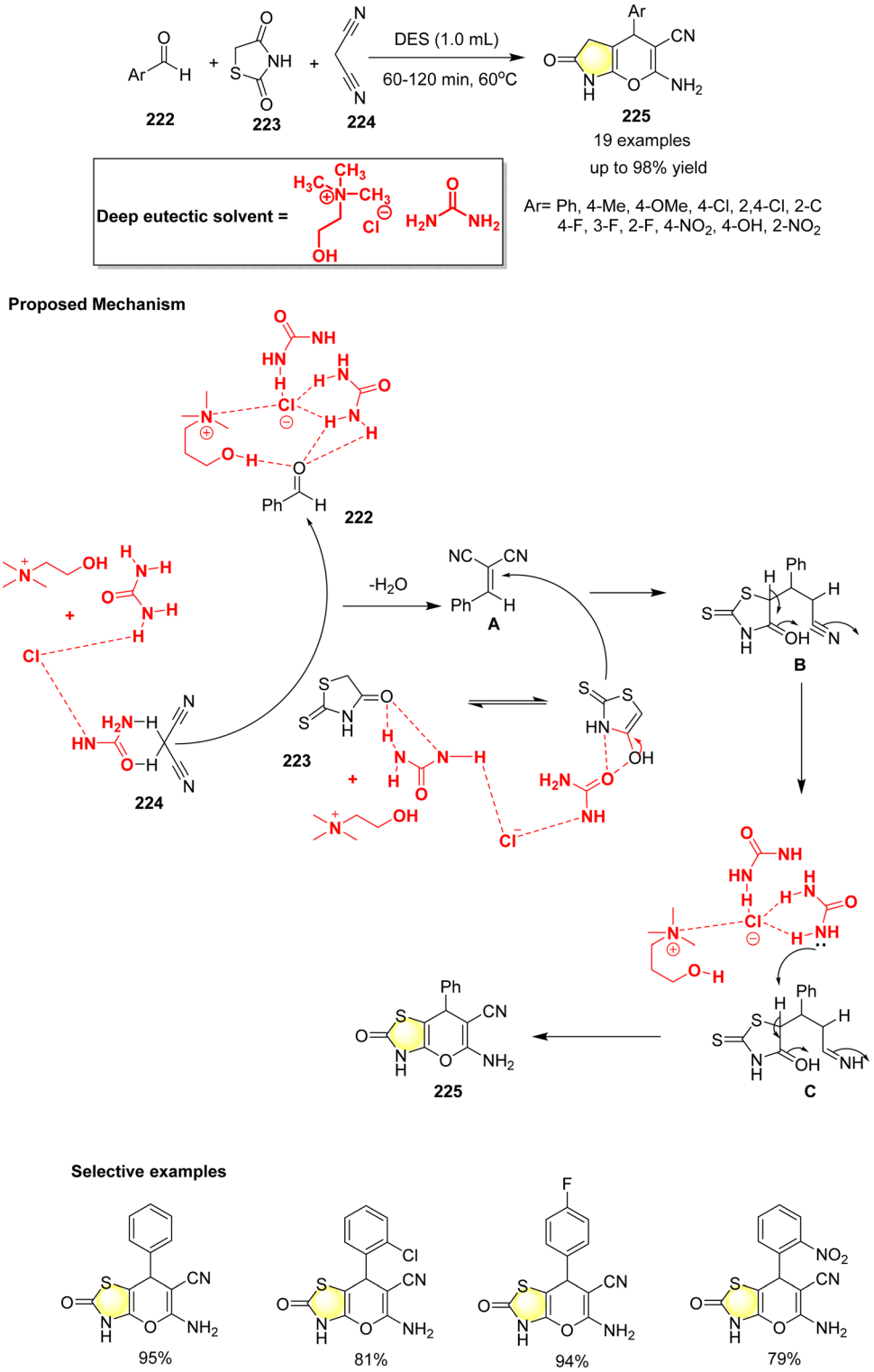
In the year 2024, Troung *et al.*[128] implemented a novel and environmentally responsible process for synthesizing 2-substituted benzothiazole derivatives **211**, employing a deep eutectic solvent (DES) composed of [CholineCl][Imidazole]$_2$. This DES served functioned simultaneously as the catalyst and solvent in a one-pot multicomponent reaction involving *o*-chloronitrobenzene **208**, aldehydes or aryl ketones **209**, and sulfur **210**, all under solvent-free conditions. The protocol yielded up to 78%, avoided toxic solvents and metals, and showed good atom economy and eco-score, aligning with green chemistry principles.

The proposed mechanism is shown in Scheme 51. The DES catalyst [CholineCl][Imidazole]$_2$ activates octasulfur **210**, generating nucleophile **A**. Nucleophile **A** attacks the carbonyl of aldehydes or aryl ketones **209** to form intermediate **B** *via* a dipolar tetrahedral intermediate **C**. Intermediate **D** then undergoes substitution with *o*-chloronitrobenzene **208**, eliminating Cl^- to form intermediate **E**. The catalyst further facilitates SO_3^- reduction and S_6 elimination, leading to cyclization of intermediate **F** and formation of 2-substituted benzothiazole derivatives **211**. The study showcases the potential of DESs offering eco-friendly substitutes for traditional solvents and ionic liquids during heterocyclic synthesis.

In 2022, Zhao *et al.*[129] outlined a clean and efficient method for synthesizing structurally unique ferrocene-linked thiazole derivative **214**. The Hantzsch reaction between ferrocene derivative bearing a bromo acetyl group **212** and diverse aryl thioureas and substituted indole/carbazole-based carbothioamides **213**. Specifically, the reaction was carried out using choline chloride/glycerol (ChCl/Gly) in a 1 : 2 molar ratio at 80 °C, eliminating the need for conventional volatile organic solvents.

The proposed mechanism for the synthesis of the title compounds in ChCl/Gly is shown in Scheme 52. The reaction likely initiates with the nucleophilic attack of aryl thioureas or substituted indole/carbazole carbothioamides **213** on the bromo acetyl group **212**, forming intermediate **A** with the elimination of HBr. The interaction of ChCl/Gly with the carbonyl oxygen increases the electrophilicity of the bromo

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.



Scheme 55 Synthesis of thiazole using choline chloride–urea-based DES.

acetyl group, facilitating this attack. This is followed by intramolecular cyclization involving the imine nitrogen and carbonyl carbon to generate intermediate **B.** Extensive hydrogen bonding with the DES activates intermediate **A**, enhancing the cyclization rate, while the resulting hydroxyl group further interacts with the DES to promote water elimination and form the unique ferrocene-linked thiazole derivative **214**. Notably, the deep eutectic solvent (DES) system demonstrated good recyclability, maintaining its efficiency over three successive cycles with minimal reduction in yield. The overall approach provides

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM. This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

multiple appealing benefits, such as an environmentally friendly and benign reaction environment, straightforward experimental procedures, easy product isolation, and high product yields. Furthermore, preliminary *in vitro* antibacterial screening of the synthesized compounds indicated that halo-substituted derivatives (F, Cl, Br), particularly compound **214f** with a fluorine substituent, exhibited strong antibacterial potential against representative Gram-positive (*B. subtilis*) and Gram-negative (*E. coli*) microbes. Compound **214f** demonstrated enhanced microbial inhibition relative to ciprofloxacin, with nearly twice the potency based on MIC assessment.

In 2021, Kaldareh *et al.*[130] described the synthesis of various 4-phenylthiazole-based hydrazine derivatives **218** that were generated using a one-pot, three-reactant protocol involving various ketones or aldehydes **215**, halogenated acetophenone intermediates **216**, as well as thiosemicarbazide **217**, utilizing a deep eutectic solvent (DES) blend of choline chloride and urea under specified conditions at 70 °C. This environmentally friendly protocol employs a cost-effective catalytic medium, offering various favourable outcomes, including remarkable synthetic output, excellent product yields within feasible reaction intervals, and overall synthetic simplicity (Scheme 53).

In 2012, Lobo *et al.*[131] designed a new, efficient, and eco-conscious synthetic route for a range of methyl thiazoles and amino-thiazole derivatives **221**, utilizing biocatalysis in combination with deep eutectic solvent (DES) technology. This pioneering work highlighted the use of lipase enzymes along with choline chloride–urea-based DES as sustainable catalytic systems involving the transformation of functionalized phenacyl bromide derivatives **219** with substituted forms of sulfur analogue of urea and sulfur-containing acetamide **220** under aqueous, room-temperature conditions (Scheme 54). The strategy ensures remarkable efficiency, delivering superior yields within a brief reaction duration, recyclable catalysts, and the elimination of toxic organic solvents and metal-based catalysts. Notably, the DES employed is prepared *via* a simple heating method without generating any by-products, underscoring its atom economy and eco-compatibility. Furthermore, the scalability and reusability of both catalysts affirm the industrial applicability of this green protocol. This work demonstrates a noteworthy contribution to the field of green synthesis, offering a dual catalytic platform that is not only operationally simple but also aligned with the principles of sustainable chemistry.

Recently, in 2025, Mohammad *et al.*[132] proposed an environmentally benign approach utilizing a single-step, three-component reaction for synthesizing fused pyran-thiazole compounds **225a–m** employing deep eutectic solvents (DESs). The reaction, involving aromatic aldehydes **222**, thiazolidinediones **223**, and malononitrile **224**, within a DES composed of choline chloride and urea, the reaction proceeds smoothly under moderate conditions, affording superior yields (up to 98% yield).

Based on previous findings, a proposed mechanism for the three-component synthesis of fused pyran-thiazole compounds **225** in a DES is illustrated in Scheme 55. Initially, aromatic aldehydes **222** are activated by hydrogen bonding within the DES, which serves as both catalyst and reaction medium, allowing condensation with malononitrile **224** to form the Knoevenagel adduct *via* C=C bond formation **A**. The adduct then undergoes nucleophilic addition with thiazolidinediones **223**, followed by intramolecular cyclization and proton transfer to yield the final products **225**. The study highlights that the strong hydrogen-bonding interactions and ionic nature of DES facilitate carbonyl activation, promoting key steps including Knoevenagel condensation, Michael addition, and cyclization. The deep eutectic solvent (DES) serves in a bifunctional capacity as both catalyst and solvent, demonstrating consistent reusability, unwavering efficiency over repeated cycles, and contributing to eco-conscious and resource-efficient synthesis.

In addition, Table 1 offers a clear, quantitative comparison by summarizing the main reaction parameters of the non-IL methods discussed earlier, along with the IL- and DES-based

Table 1 Comparative evaluation of ILs, DESs, and conventional methods for thiazole synthesis[a]

Entry	Method	Reaction time (min)	Yield (%)	Cost	Toxicity	Recycl-ability	Reference number
1	Conventional	55–190	55–96	Medium	Low	NR	117
2	Conventional	120	33–93	Medium	Medium	NR	118
3	Conventional	15–30	91–96	Medium	Low	Up to 8 cycles	119
4	Conventional	10	78–97	Medium	Low	Up to 5 cycles	121
5	Conventional	120–240	87–90	Low–medium	Low	Up to 3 cycles	122
6	Conventional	2800	31–96	Medium–high	Medium	NR	123
7	Conventional	4–22	Up to 98	Low	Low	Up to 4 cycles	124
8	Conventional	15–30	92–98	Medium–high	Low	Up to 8 cycles	125
9	DES	10–35	83–95	Low	Low	Up to 4 cycles	126
10	DES	360	Up to 78	Low	Low	Up to 3 cycles	128
11	DES	360	74–91	Low	Low	Up to 3 cycles	129
12	DES	45–80	90–97	Low	Low	NR	130
13	DES	15–25	81–98	Low	Low	Up to 4 cycles	131
14	DES	60–120	64–98	Low	Low	Up to 7 cycles	132

[a] NR: not reported.

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM. This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

reactions reported here. It highlights differences in reaction efficiency, yield, cost, toxicity, and recyclability.

The comparison in Table 1 indicates that although non-IL and DES-based approaches provide benefits such as lower toxicity and operational simplicity, IL-mediated systems generally demonstrate higher recyclability, efficiency, and product yield. These findings highlight that the most effective approach to sustainable thiazole synthesis is one that balances eco-friendliness with catalytic efficiency, supporting further advances in green heterocyclic chemistry.

4.5. Green chemistry metrics assessment

Green chemistry metrics serve as essential tools for quantitatively assessing the environmental sustainability of chemical transformations.[133] In this section, various parameters such as percentage yields, atom economy, process mass intensity (PMI),

Table 2 Green chemistry metrics for ionic liquid-mediated thiazole synthesis[a]

Entry	Yield (%)	AE (%)	E-factor	PMI	RME (%)	Recyclability	Limitation	Toxicity	Reference number
1	71–83	NR	NR	NR	NR	Up to 3 cycles	Green chemistry metrics not reported	Low	72
2	87–96	NR	NR	NR	NR	Up to 3 cycles	Green chemistry metrics not reported	Low	73
3	77–99	NR	NR	NR	NR	Limited	Green chemistry metrics not reported	Low	74
4	75–92	NR	NR	NR	NR	NR	Green chemistry metrics not reported	Low	75
5	76–97	NR	NR	NR	NR	Up to 3 cycles	Green chemistry metrics not reported	Low	76
6	80–90	NR	NR	NR	NR	Up to 5 cycles	Green chemistry metrics not reported	Low	77
7	82–96	NR	NR	NR	NR	NR	Green chemistry metrics not reported	NR	78
8	85–96	NR	NR	NR	NR	Up to 2 cycles	Green chemistry metrics not reported	Low	79
9	Up to 97	NR	NR	NR	NR	Up to 3 cycles	Green chemistry metrics not reported	Low	80
10	77–94	NR	NR	NR	NR	Up to 3 cycles	Green chemistry metrics not reported	Low	81
11	79–96	NR	NR	NR	NR	Limited	Green chemistry metrics not reported	Low	82
12	Up to 90	NR	NR	NR	NR	Up to 2 cycles	Green chemistry metrics not reported	Low	83
13	70–93	NR	NR	NR	NR	Up to 4 cycles	Green chemistry metrics not reported	Low	84
14	Up to 99	NR	NR	NR	NR	Up to 5 cycles	Green chemistry metrics not reported	Low	85
15	83–95	NR	NR	NR	NR	Up to 5 cycles	Green chemistry metrics not reported	Low	89
16	82–96	NR	NR	NR	NR	Up to 3 cycles	Green chemistry metrics not reported	Low	91
17	60–88	NR	NR	NR	NR	Up to 5 cycles	Green chemistry metrics not reported	Low	92
18	81–92	NR	NR	NR	NR	NR	Green chemistry metrics not reported	Medium	93
19	70–82	NR	NR	NR	NR	NR	Green chemistry metrics not reported	Low	94
20	88–98	NR	NR	NR	NR	Up to 7 cycles	Green chemistry metrics not reported	Low	95
21	86–93	NR	NR	NR	NR	Up to 6 cycles	Green chemistry metrics not reported	Low	96
22	86–92	NR	NR	NR	NR	Up to 4 cycles	Green chemistry metrics not reported	Medium	97
23	72–90	NR	NR	NR	NR	NR	Green chemistry metrics not reported	NR	98
24	80–86	NR	NR	NR	NR	NR	Green chemistry metrics not reported	Medium	99
25	80–92	NR	NR	NR	NR	Up to 5 cycles	Green chemistry metrics not reported	Low	100
26	76–95	NR	NR	NR	NR	Up to 6 cycles	Green chemistry metrics not reported	Low	101
27	72–90	NR	NR	NR	NR	NR	Green chemistry metrics not reported	NR	102
28	75–98	NR	NR	NR	NR	Up to 5 cycles	Green chemistry metrics not reported	Low	104
29	88–98	NR	NR	NR	NR	Up to 5 cycles	Green chemistry metrics not reported	Low	105
30	85–98	NR	NR	NR	NR	Up to 5 cycles	Green chemistry metrics not reported	Low	107
31	87–96	NR	NR	NR	NR	Up to 6 cycles	Green chemistry metrics not reported	Low	108
32	75–92	NR	NR	NR	NR	Up to 5 cycles	Green chemistry metrics not reported	Low	109
33	84–95	NR	NR	NR	NR	Up to 5 cycles	Green chemistry metrics not reported	Low	110
34	Up to 90	NR	NR	NR	NR	NR	Green chemistry metrics not reported	NR	111
35	Up to 99	NR	NR	NR	NR	Up to 7 cycles	Green chemistry metrics not reported	Low	112
36	57–93	NR	NR	NR	NR	Up to 8 cycles	Green chemistry metrics not reported	Low	113
37	55–96	NR	NR	NR	NR	NR	Green chemistry metrics not reported	NR	117
38	33–93	NR	NR	NR	NR	NR	Green chemistry metrics not reported	NR	118
39	91–96	NR	NR	NR	NR	Up to 8 cycles	Green chemistry metrics not reported	Low	119
40	78–97	NR	NR	NR	NR	Up to 5 cycles	Green chemistry metrics not reported	Low	121
41	87–90	NR	NR	NR	NR	Up to 3 cycles	Green chemistry metrics not reported	Low	122
42	31–96	NR	NR	NR	NR	NR	Green chemistry metrics not reported	NR	123
43	Up to 98	NR	NR	NR	NR	Up to 4 cycles	Green chemistry metrics not reported	Low	124
44	92–98	NR	NR	NR	NR	Up to 8 cycles	Green chemistry metrics not reported	Low	125
45	83–95	NR	NR	NR	NR	Up to 4 cycles	Green chemistry metrics not reported	Low	126
46	**Up to 78**	**64.54**	**0.61**	**1.98**	**50.34**	**Up to 3 cycles**	**None**	**Low**	**128**
47	74–91	NR	NR	NR	NR	Up to 3 cycles	Green chemistry metrics not reported	Low	129
48	90–97	NR	NR	NR	NR	NR	Green chemistry metrics not reported	Low	130
49	**81–98**	**100**	**NR**	**NR**	**NR**	**Up to 4 cycles**	**Limited**	**Low**	**131**
50	64–98	NR	NR	NR	NR	Up to 7 cycles	Green chemistry metrics not reported	Low	132

[a] NR: not reported, AE: atom economy, E-factor: environmental factor; RME: reaction mass efficiency; PMI: process mass intensity.

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM. This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

E-factor, and reaction mass efficiency (RME) are considered to determine how efficiently the starting materials are transformed into target products with minimal waste formation. These metrics are analyzed based on reported literature data to assess the overall sustainability of ionic liquid-mediated thiazole synthesis routes, as summarized in Table 2.

The analysis of green chemistry metrics clearly demonstrates that ionic liquid-mediated thiazole syntheses offer significant advantages in terms of sustainability over conventional solvent-based methods. Most reported studies demonstrate high atom economy, reduced E-factor, and favourable PMI values, reflecting efficient utilization of reactants and minimal waste generation. Furthermore, the ability to recycle ionic liquids and their dual function as solvents and catalysts contribute to improved process efficiency and environmental friendliness, highlighting their promise for sustainable and practical thiazole synthesis.

5. Conclusion

In conclusion, ionic liquids (ILs) have gained widespread recognition as versatile and environmentally friendly media for synthesizing thiazole derivatives, offering significant advantages in terms of reaction efficiency, selectivity, and catalyst recyclability. This review organizes IL-mediated thiazole syntheses by their functional roles, spanning from passive green solvents to dual-role catalytic systems and supported IL platforms, highlighting their adaptability in promoting various synthetic pathways. A comparative analysis with non-IL green alternatives like deep eutectic solvents (DESs) and biocatalytic systems shows the complementary nature of these approaches within the broader context of sustainable chemistry. However, challenges such as the high cost and complex preparation of some task-specific ILs remain areas for improvement. Future research should prioritize developing bio-based and low-toxicity ILs, scaling up IL-mediated protocols for industrial use, and integrating IL systems with other green technologies such as flow chemistry and renewable energy sources. Additionally, exploring the underlying mechanisms of IL-mediated reactions and designing recyclable, broadly applicable IL systems may pave the way for their expanded use in diverse areas of heterocyclic chemistry. By consolidating scattered literature and providing a focused, functional classification, this review not only addresses a critical gap but also lays the foundation for future innovation. This study aims to inform and inspire the development of eco-efficient and industrially relevant strategies for constructing thiazole-based compounds.

Conflicts of interest

All authors declared that there were no conflicts of interest to declare.

Data availability

This is a review article; hence, no primary research results, software, or code have been included, and no new data were generated or analyzed as part of this review.

Acknowledgements

The authors thank the Science and Engineering Research Board, India, for the funding provided through YSS/2015/000450, the Chancellor of VIT for providing an opportunity to carry out this study, and VIT for providing the 'VIT SEED Grant-RGEMS Fund (SG20220031, SG20240023)' for carrying out this research work.

References

1 Y. Gu and F. Jérôme, *Chem. Soc. Rev.*, 2013, **42**, 9550–9570.
2 P. Anastas and N. Eghbali, *Chem. Soc. Rev.*, 2010, **39**, 301–312.
3 M. Dinodia, in *Strategies for the Synthesis of Heterocycles and Their Applications*, ed. P. Kumari and A. B. Patel, IntechOpen, Rijeka, Croatia, 1st edn, 2022, ch.10.
4 B. Wang, M. Li, S. Zhang, H. Wu, Y. Liao and H. Li, *Appl. Catal., B*, 2023, **327**, 122454.
5 M. Kazemi and N. Karezani, *Biol. Mol. Chem.*, 2023, **1**, 15–26.
6 R. M. Sultanova, A. N. Lobov, A. V. Shumadalova, S. A. Meshcheryakova, Z. R. Zileeva, N. S. Khusnutdinova, V. A. Vakhitov and Y. V. Vakhitova, *Nat. Prod. Res.*, 2021, **35**, 1340–1348.
7 L. Yurttaş, A. E. Evren and Y. Özkay, *Eur. J. Life Sci.*, 2022, **1**, 8–19.
8 A. A. Kiryanov, P. Sampson and A. J. Seed, *J. Org. Chem.*, 2001, **66**, 925–7929.
9 B.-Y. Kim, H.-S. Kim and A. Helal, *Sens. Actuators, B*, 2015, **206**, 430–434.
10 M. Metwally, *Dyes Pigm.*, 2004, **60**, 249–264.
11 V. E. Borisenko, A. Koll, E. E. Kolmakov and A. G. Rjasnyi, *J. Mol. Struct.*, 2006, **783**, 101–115.
12 A. Dondoni, *Org. Biomol. Chem.*, 2010, **8**, 3366–3385.
13 K. Kant, C. K. Patel, S. Banerjee, P. Naik, A. K. Atta, A. K. Kabi and C. C. Malakar, *ChemistrySelect*, 2023, **8**, e202303988.
14 Z.-X. Niu, Y.-T. Wang, S.-N. Zhang, Y. Li, X.-B. Chen, S.-Q. Wang and H.-M. Liu, *Eur. J. Med. Chem.*, 2023, **250**, 115172.
15 T. T. H. Van, H. N. K. Nguyen, P. M. Smooker and P. J. Coloe, *Int. J. Food Microbiol.*, 2012, **154**, 98–106.
16 H. S. Lo, K. P. Y. Hui, H.-M. Lai, X. He, K. S. Khan, S. Kaur, J. Huang, Z. Li, A. K. N. Chan, H. H.-Y. Cheung, K.-C. Ng, J. C. W. Ho, Y. W. Chen, B. Ma, P. M.-H. Cheung, D. Shin, K. Wang, M.-H. Lee, B. Selisko, C. Eydoux, J.-C. Guillemot, B. Canard, K.-P. Wu, P.-H. Liang, I. Dikic, Z. Zuo, F. K. L. Chan, D. S. C. Hui, V. C. T. Mok, K.-B. Wong, C. K. P. Mok, H. Ko, W. S. Aik, M. C. W. Chan and W.-L. Ng, *ACS Cent. Sci.*, 2021, **7**, 792–802.
17 Q. Sun, F. Ye, H. Liang, H. Liu, C. Li, R. Lu, B. Huang, L. Zhao, W. Tan and L. Lai, *Signal Transduction Targeted Ther.*, 2021, **6**, 212.
18 L. Xu, H. Liu, B. P. Murray, C. Callebaut, M. S. Lee, A. Hong, R. G. Strickley, L. K. Tsai, K. M. Stray, Y. Wang, G. R. Rhodes and M. C. Desai, *ACS Med. Chem. Lett.*, 2010, **1**, 209–213.
19 I. T. Humedy, *Tikrit J. Pure Sci.*, 2023, **20**, 97–104.

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM. This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

20 J. F. Rossignol, S. L. Frazia, L. Chiappa, A. Ciucci and M. G. Santoro, *J. Biol. Chem.*, 2009, **284**, 29798–29808.
21 C. M. Chan, X. Jing, L. A. Pike, Q. Zhou, D.-J. Lim, S. B. Sams, G. S. Lund, V. Sharma, B. R. Haugen and R. E. Schweppe, *Clin. Cancer Res.*, 2012, **18**, 3580–3591.
22 Y. Matsunaga, T. Tanaka, K. Yoshinaga, S. Ueki, Y. Hori, R. Eta, Y. Kawabata, K. Yoshii, K. Yoshida, T. Matsumura, S. Furuta, M. Takei, J. ack and Z. Itoh, *J. Pharmacol. Exp. Ther.*, 2011, **336**, 791–800.
23 T. Furugohri, K. Isobe, Y. Honda, C. Kamisato-Matsumoto, N. Sugiyama, T. Nagahara, Y. Morishima and T. Shibano, *J. Thromb. Haemostasis*, 2008, **6**, 1542–1549.
24 T. Nagata, T. Yoshino, N. Haginoya, K. Yoshikawa, M. Nagamochi, S. Kobayashi, S. Komoriya, A. Yokomizo, R. Muto, M. Yamaguchi, K. Osanai, M. Suzuki and H. Kanno, *Bioorg. Med. Chem.*, 2009, **17**, 1193–1206.
25 A. Bekker, C. Kloepping and S. Collingwood, *J Anaesthesiol Clin Pharmacol.*, 2018, **34**, 450–457.
26 Y. Takano, K. Hase-Aoki, H. Horiuchi, L. Zhao, Y. Kasahara, S. Kondo and M. A. Becker, *Life Sci.*, 2005, **76**, 835–1847.
27 L. G. Sánchez-Lozada, E. Tapia, V. Soto, C. Ávila-Casado, M. Franco, J. L. Wessale, L. Zhao and R. J. Johnson, *Nephron Physiol.*, 2008, **108**, 69–78.
28 T. Wilhoit, J. M. Patrick and M. B. May, *J. Adv. Pract. Oncol.*, 2020, **11**, 768–775.
29 A. Ayati, S. Emami, A. Asadipour, A. Shafiee and A. Foroumadi, *Eur. J. Med. Chem.*, 2015, **97**, 699–718.
30 S. Ahmad, M. Z. Alam, U. Salma, M. Mohasin, P. F. Rahaman, H. Parveen and S. A. Khan, *J. Mol. Struct.*, 2024, **1312**, 138438.
31 S. Mohurle and B. Maiti, *ChemistrySelect.*, 2025, **10**, e202404377.
32 C. B. Mishra, S. Kumari and M. Tiwari, *Eur. J. Med. Chem.*, 2015, **92**, 1–34.
33 P. Iyer, J. Bolla, V. Kumar, M. S. Gill and M. E. Sobhia, *Mol. Divers.*, 2015, **19**, 855–870.
34 A.-M. Borcea, I. Ionu□, O. Crişan and O. Oniga, *Molecules*, 2021, **26**, 624.
35 A. V. Moradi, A. A. Peyghan, S. Hashemian and M. T. Baei, *Bull. Korean Chem. Soc.*, 2012, **33**, 3285–3292.
36 A. El-Mekabaty, O. M. O. Habib, E. B. Moawad and A. M. Hasel, *J. Heterocycl. Chem.*, 2016, **53**, 1214–1221.
37 A. H. Abdelazeem, S. I. Khan, S. W. White, K. J. Sufka and C. R. McCurdy, *Bioorg. Med. Chem.*, 2015, **23**, 3248–3259.
38 S. Pola, in *Scope of Selective Heterocycles from Organic and Pharmaceutical Perspective,* ed. R. Varala, IntechOpen, Rijeka, Croatia, 1st edn, 2016, ch. 1.
39 C. J. Mallia, L. Englert, G. C. Walter and I. R. Baxendale, *Beilstein J. Org. Chem.*, 2015, **11**, 875–883.
40 K. M. Weiß, S. Wei and S. B. Tsogoeva, *Org. Biomol. Chem.*, 2011, **9**, 3457–3461.
41 A. Grozav, L. Găină, V. Pileczki, O. Crisan, L. Silaghi-Dumitrescu, B. Therrien, V. Zaharia and I. Berindan-Neagoe, *Int. J. Mol. Sci.*, 2014, **15**, 22059–22072.
42 A. H. S. Neves, D. S. da Silva, G. M Siqueira, G. D. Gamaro, W. Cunico and A. L. da Silva, *Med. Chem. Res.*, 2018, **27**, 186–193.
43 Y.-J. Wu, in *Metalation of Azoles and Related Five-Membered Ring Heterocycles*, ed. G. W. Gribble, Springer, Berlin, Heidelberg, 1st edn, 2012, pp. 307–327.
44 A. Leoni, A. Locatelli, R. Morigi and M. Rambaldi, *Expert Opin. Ther. Pat.*, 2014, **24**, 201–216.
45 A. Petrou, M. Fesatidou and A. Geronikaki, *Molecules*, 2021, **26**, 3166.
46 H. T. Clarke and S. Gurin, *J. Am. Chem. Soc.*, 1935, **57**, 876–1881.
47 N. Asao and Y. Yamamoto, *Bull. Chem. Soc. Jpn.*, 2000, **73**, 1071–1087.
48 B. A. Trofimov, S. E. Korostova, L. N. Balabanova and A. I. Mikhaleva, *Khim. Geterotsikl. Soedin.*, 1975, 177–301.
49 A. H. Cook, I. Heilbron and A. L. Levy, *J. Chem. Soc.*, 1947, 1594–1598.
50 M. Alam, S. Khan and M. Shaheen Khan, *J. Chil. Chem. Soc.*, 2008, **53**, 1714–1717.
51 *Heterocyclic Chemistry in Drug Discovery*, ed J. J. Li, Wiley-Blackwell, Hoboken, 1st edn, 2013.
52 S. H. Ali and A. R. Sayed, *Synth. Commun.*, 2021, **51**, 670–700.
53 S. Gabriel, *Bibliogr. Chim.*, 1910, **43**, 1283–1287.
54 S. B. Yoon, E. J. Chun, Y. R. Noh, Y. J. Yoon and S.-G. Lee, *Bull. Korean Chem. Soc.*, 2013, **34**, 2819–2821.
55 S. Sharma, S. Gangal and A. Rauf, *Rasayan J. Chem.*, 2008, **1**, 693–717.
56 P. J. Dunn, *Chem. Soc. Rev.*, 2012, **41**, 1452–1461.
57 F. Karadas, M. Atilhan and S. Aparicio, *Energy Fuels*, 2010, **24**, 5817–5828.
58 J. S. Wilkes, P. Wasserscheid and T. Welton, in *Ionic Liquids in Synthesis*, eds. P. Wasserscheid and T. Welton, Wiley-VCH, Weinheim, 2nd edn, 2008, ch. 1.
59 N. V. Plechkova and K. R. Seddon, *Chem. Soc. Rev.*, 2008, **37**, 123–150.
60 W. Beichel, Y. Yu, G. Dlubek, R. Krause-Rehberg, J. Pionteck, D. Pfefferkorn, S. Bulut, D. Bejan, C. Friedrich and I. Krossing, *Phys. Chem. Chem. Phys.*, 2013, **15**, 8821–8830.
61 P. S. V. Kumar, L. Suresh, G. Bhargavi, S. Basavoju and G. V. P. Chandramouli, *ACS Sustain. Chem. Eng.*, 2015, **3**, 2944–2950.
62 T. Itoh, *Chem. Rev.*, 2017, **117**, 10567–10607.
63 L. Wang, H. Li and P. Li, *Tetrahedron*, 2009, **65**, 364–368.
64 A. Jordan and N. Gathergood, *Chem. Soc. Rev.*, 2015, **4**, 8200–8237.
65 P. C. Marr and A. C. Marr, *Green Chem.*, 2016, **18**, 105–128.
66 *Ionic Liquids (ILs) in Organometallic Catalysis*, ed. J. Dupont and L. Kollár, Springer-Verlag, Berlin, Heidelberg, 1st edn, 2015, p. 353.
67 B. L. Gadilohar and G. S. Shankarling, *J. Mol. Liq.*, 2017, **227**, 234–261.
68 S. Khandelwal, Y. K. Tailor and M. Kumar, *J. Mol. Liq.*, 2016, **215**, 345–386.
69 A. T. A. Imeer, A. A. H. Kadhum, S. D. Ahmed, H. A. Al-Bahrani, R. M. Mhaibes and G. Shu, *Appl. Organomet. Chem.*, 2025, **39**, e7819.

© 2025 The Author(s). Published by the Royal Society of Chemistry

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM. This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

70 Z. A. Kaplancikli, M. D. Altıntop, O. Atli, B. Sever, M. Baysal, H. E. Temel, F. Demirci and A. Ozdemir, *Anticancer Agents Med. Chem.*, 2017, **17**, 674–681.
71 N. Kaur, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2019, **194**, 165–185.
72 R. Hou, H. Wanga, H. Tsai and L. Chen, *J. Chin. Chem. Soc.*, 2006, **53**, 863–866.
73 T. M. Potewar, S. A. Ingale and K. V. Srinivasan, *Tetrahedron*, 2007, **63**, 11066–11069.
74 Y. Izumisawa and H. Togo, *Green Sustainable Chem.*, 2011, **1**, 54–62.
75 M. K. Muthyala and A. Kumar, *J. Heterocycl. Chem.*, 2012, **49**, 959–964.
76 A. S. Shahvelayati, I. Yavari and A. S. Delbari, *Chin. Chem. Lett.*, 2014, **25**, 119–122.
77 M. A. Waseem, Shireen, A. Srivastava, A. Srivastava, Rahila and I. R. Siddiqui, *J. Saudi Chem. Soc.*, 2015, **19**, 334–339.
78 J. Ramprasad, N. Nayak, U. Dalimba, P. Yogeeswari and D. Sriram, *MedChemComm*, 2016, **7**, 338–344.
79 A. S. Shahvelayati, A. Ashouri and A. S. Delbari, *Lett. Org. Chem.*, 2016, **13**, 100–106.
80 A. S. Shahvelayati, L. Hajiaghababaei and A. P. Sarmad, *Iran. Chem. Commun.*, 2017, **5**, 262–267.
81 R. Nadaf, *J. Mol. Catal. A:Chem.*, 2004, **214**, 155–160.
82 M. B. Maradolla, S. K. Allam, A. Mandha and G. V. P. Chandramouli, *Arkivoc*, 2008, **2008**, 42–46.
83 A. K. Yadav, G. R. Sharma, P. Dhakad and T. Yadav, *Tetrahedron Lett.*, 2012, **53**, 859–862.
84 L. D. Khillare, M. R. Bhosle, A. R. Deshmukh and R. A. Mane, *Res. Chem. Intermed.*, 2015, **41**, 8955–8964.
85 X. Gao, B. Yu, Z. Yang, Y. Zhao, H. Zhang, L. Hao, B. Han and Z. Liu, *ACS Catal.*, 2015, **5**, 6648–6652.
86 C. Das Neves Gomes, O. Jacquet, C. Villiers, P. Thuéry, M. Ephritikhine and T. Cantat, *Angew. Chem., Int. Ed.*, 2012, **51**, 187–190.
87 X. Gao, B. Yu, Y. Zhao, L. Hao and Z. Liu, *RSC Adv.*, 2014, **4**, 56957–56960.
88 W. Sattler and G. Parkin, *JACS*, 2012, **134**, 17462–17465.
89 M. Hasanpour, H. Eshghi, M. Bakavoli and M. Mirzaeia, *J. Chin. Chem. Soc.*, 2015, **62**, 412–419.
90 A. Aggarwal, N. L. Lancaster, A. R. Sethi and T. Welton, *Green Chem.*, 2002, **4**, 517–520.
91 J. A. Shiran, A. Yahyazadeh, B. M. Yamin, M. Mamaghani and J. Albadi, *J. Heterocycl. Chem.*, 2016, **53**, 1009–1016.
92 I. R. Siddiqui, A. Srivastava, S. Shamim, A. Srivastava, Shireen and M. A. Waseem, *J. Heterocycl. Chem.*, 2016, **53**, 849–858.
93 A. R. Deshmukh, S. T. Dhumal, L. U. Nawale, V. M. Khedkar, D. Sarkar and R. A. Mane, *Synth. Commun.*, 2019, **49**, 587–601.
94 S. Pal, R. Chatterjee, S. Santra, G. V. Zyryanov and A. Majee, *Chem. Pap.*, 2020, **74**, 3389–3396.
95 L. Z. Fekri, H. Hamidian and M. A. Chekosarani, *RSC Adv.*, 2020, **10**, 556–564.
96 P. Kakati, P. Singh, P. Yadav and S. K. Awasthi, *New J. Chem.*, 2021, **45**, 6724–6738.
97 M. S. Mirakmahaleh, K. Rad-Moghadam, H. Kefayati and S. Falakro, *Mol. Divers.*, 2021, **25**, 109–119.
98 G. Badhani, A. Joshi and S. Adimurthy, *Eur. J. Org. Chem.*, 2021, **2021**, 6705–6716.
99 D. V. Sowbhagyam, D. Koteswararao and D. K. Prameela, *Int. J. Res. Appl. Sci. Eng. Technol.*, 2023, **11**, 200–204.
100 P. Pinate and S. Makone, *J. Sulfur Chem.*, 2023, **44**, 20–36.
101 N. A. A. Ahmad, S. B. Aher, P. R. Bhagat and P. N. Muskawar, *Res. Sq.*, 2024, DOI: **10.21203/rs.3.rs-5437620/v1**.
102 C.-Y. Chen, I. J. Barve and C.-M. Sun, *ACS Comb. Sci.*, 2016, **18**, 638–643.
103 C. B. Singh, S. Murru, V. Kavala and B. K. Patel, *Org. Lett.*, 2006, **8**, 5397–5399.
104 T. T. Nguyen, X.-T. T. Nguyen, T.-L. H. Nguyen and P. H. Tran, *ACS Omega*, 2019, **4**, 368–373.
105 H. Rostami and L. Shiri, *Mater. Today Chem.*, 2021, **20**, 100400.
106 M. M. Heravi and S. Moghimi, *Tetrahedron Lett.*, 2012, **53**, 392–394.
107 M. Kalhor and Z. Zarnegar, *Res. Chem. Intermed.*, 2022, **48**, 519–540.
108 M. Kalhor, P. Nozare, E. Vessally and B. Mohammadi, *ChemistrySelect*, 2023, **8**, e202301283.
109 M. Kalhor, Z. Vahedi and H. Gharoubi, *RSC Adv.*, 2023, **13**, 9208–9221.
110 A. Khalil, I. Mohammadpoor-Baltork, V. Mirkhani, M. Moghadam, S. Tangestaninejad, B. Notash and H. Sabzyan, *J. Mol. Liq.*, 2024, **397**, 124118.
111 R. M. Mohareb, R. A. Ibrahim and F. O. Al Farouk, *J. Iran. Chem. Soc.*, 2024, **21**, 921–942.
112 A. Aggarwal and H. K. Chopra, *Res. Chem. Intermed.*, 2025, **51**, 3301–3316.
113 M.-C. Le, N.-H. Nguyen, C.-T. Duong, Q. M. Vo and T. X. T. Luu, *Green Chem. Lett. Rev.*, 2025, **18**, 2503732.
114 A. Paiva, R. Craveiro, I. Aroso, M. Martins, R. L. Reis and A. R. C. Duarte, *ACS Sustain. Chem. Eng.*, 2014, **2**, 1063–1071.
115 R. S. Varma, *Green Chem.*, 2014, **16**, 2027.
116 B. Wang, J. Huang, H. Wu, X. Yan, Y. Liao and H. Li, *J. Energy Chem.*, 2024, **92**, 16–25.
117 J. Zhou, X. Huang, Z. Zhang, P. Song and Y. Li, *J. Biotechnol.*, 2017, **241**, 14–21.
118 I. V. Rassokhina, T. A. Tikhonova, S. G. Kobylskoy, I. Y. Babkin, V. Z. Shirinian, V. Gevorgyan, I. V. Zavarzin and Y. A. Volkova, *J. Org. Chem.*, 2017, **82**, 9682–9692.
119 A. Y. A. Alzahrani, T. N. A. Eskander, M. Saleh Hussein Alzubi, H. M. Abd El-Lateef and M. A. E. A. A. Ali El-Remaily, *Inorg. Chem. Commun.*, 2024, **165**, 112494.
120 B. Zeynizadeh, S. Rahmani and E. Eghbali, *Polyhedron*, 2019, **168**, 57–66.
121 P. Mahaur, K. Rajput, V. Singh, V. Srivastava and S. Singh, *RSC Adv.*, 2024, **14**, 21213–21218.
122 P. P. Mogle, S. S. Pohare, S. Zangade and B. S. Dawane, *J. Iran. Chem. Soc.*, 2024, **21**, 2703–2712.
123 M. Neetha, S. B. Umabharathi and G. Anilkumar, *Catal. Lett.*, 2025, **155**, 15.

Open Access Article. Published on 27 October 2025. Downloaded on 12/7/2025 8:22:11 AM.
This article is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported Licence.

124 A. Gurav, L. Bhosale, P. N. Chavan, R. Gurav, N. Nerlekar, P. Dandge, S. Rochlani, S. Sankpal and S. Hangirgekar, *J. Mol. Struct.*, 2025, **1338**, 142223.
125 M. A. E. A. A. Ali El-Remaily, O. Elhady, A. Abdou, D. Alhashmialameer, T. N. A. Eskander and A. M. Abu-Dief, *J. Mol. Struct.*, 2023, **1292**, 136188.
126 E. Chegeni, D. Habibi, A. Monem and Z. Jahaniyan, *Sci. Rep.*, 2025, **15**, 7508.
127 N. Basirat, S. S. Sajadikhah and A. Zare, *Res. Chem. Intermed.*, 2020, **46**, 3263–3275.
128 V. A. Truong, M. H. Tran, T. H. Nguyen and H. T. Nguyen, *RSC Adv.*, 2024, **14**, 39462–39471.
129 D. Zhao, Y. Liu, Y. Li and Y. Chen, *RSC Adv.*, 2022, **12**, 22054–22059.
130 M. Foroughi Kaldareh, M. Mokhtary and M. Nikpassand, *Polycyclic Aromat. Compd.*, 2021, **41**, 1012–1019.
131 H. R. Lobo, B. S. Singh and G. S. Shankarling, *Catal. Lett.*, 2012, **142**, 1369–1375.
132 F. Mohammad, N. Azizi, Z. Mirjafari and J. Mokhtari, *J. Ionic Liq.*, 2025, **5**, 100157.
133 M. Tobiszewski, M. Marć, A. Gałuszka and J. Namieśnik, *Molecules*, 2015, **20**, 10928–10946.

© 2025 The Author(s). Published by the Royal Society of Chemistry