IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 8, April 2026
Impact Factor: 8.2

Synthetic Strategies for the Construction of Polyhydroquinoline Frameworks: A Review

Baliram T. Vibhute[1], Amol J. Ghoti[1], Mahesh R. Walle [2], Abhijeet S. Patki[3*]
[1]Doshi Vakil Arts College and GCUB Science & Commerce Goregaon-Raigad Maharashtra (India).
[2]Sundarrao More Arts, Commerce and Science College, Poladpur-Raigad, Maharashtra (India).
[3]Shivaji Mahavidyalaya Renapur-413527, Dist-Latur, Maharashtra (India).
*Corresponding Author: abhijeetpatki007@gmail.com

Abstract: *Polyhydroquinolines represent an important class of heterocyclic compounds due to their significant biological and pharmacological activities, including antihypertensive, antimicrobial, anticancer, and anti-inflammatory properties. Consequently, the development of efficient and sustainable methods for their synthesis has attracted considerable attention in modern organic chemistry. Multicomponent reactions (MCRs), particularly the Hantzsch reaction, have emerged as powerful synthetic tools for constructing polyhydroquinoline frameworks because they enable the formation of complex molecules in a single step with high atom economy, operational simplicity, and reduced reaction time.*

This review summarizes recent advances in the synthesis of polyhydroquinoline derivatives using environmentally friendly catalytic systems and green chemistry approaches. Various catalytic strategies, including heterogeneous catalysts, nanocatalysts, metal-supported catalysts, and recyclable catalytic systems, have been explored to enhance reaction efficiency and product yield under mild conditions. In addition, solvent-free, catalyst-free, microwave-assisted, and deep eutectic solvent-based methodologies have been reported as sustainable alternatives for the synthesis of these compounds.

Overall, these approaches highlight the growing importance of green and sustainable catalytic strategies for the efficient synthesis of polyhydroquinoline derivatives with potential pharmaceutical and industrial applications.

Keywords: Polyhydroquinolines; Multicomponent reactions; Hantzsch reaction; Green chemistry; Heterogeneous catalysts; Nanocatalysts; Sustainable synthesis

1. Introduction

The demand for sustainable and high-yielding synthetic methodologies for the construction of biologically significant molecular frameworks continues to grow in modern organic chemistry [1]. In this context, multicomponent reactions (MCRs) have proven to be exceptionally valuable, as they enable the rapid generation of structurally complex compounds through one-pot processes [2,3]. These transformations integrate three or more reactants into a single operation, minimizing purification steps and maximizing resource efficiency. Compared with traditional sequential synthetic routes, MCRs provide superior atom economy and reduced reaction time, thereby aligning closely with the principles of green chemistry.

The philosophy of green chemistry emphasizes the development of environmentally responsible chemical processes that reduce waste, toxicity, and energy consumption [4]. To achieve these objectives, the implementation of recyclable catalytic systems has become increasingly important. Heterogeneous catalysts, in particular, offer distinct advantages such as simple recovery, operational stability, and repeated reuse without significant loss of activity [5,6]. Their performance is often enhanced by strong interactions between the catalytically active phase and the support surface, which influence dispersion, stability, and catalytic efficiency [6].

ISSN: 2581-9429 Volume 6, Issue 8, April 2026 Impact Factor: 8.2

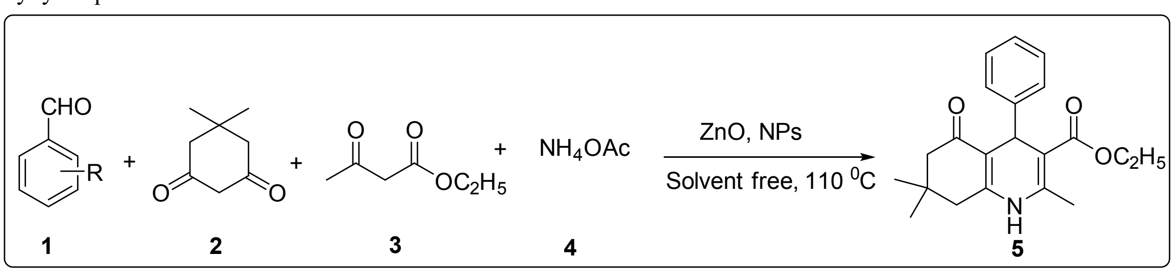
Zirconia (ZrO_2) has emerged as an attractive support material in heterogeneous catalysis due to its high thermal resistance, mechanical robustness, chemical inertness, and recyclability [7–9]. Zirconia-supported systems have demonstrated effectiveness in various organic transformations, including carbon–carbon bond-forming reactions and epoxidation processes [10,11]. The uniform distribution of active species over the zirconia surface enhances catalytic accessibility and durability, contributing to improved reaction outcomes [12]. Among sustainable catalytic metals, iron occupies a prominent position because of its abundance, low toxicity, and economic viability [13]. Iron-based catalysts have been widely applied in numerous organic transformations, such as nucleophilic substitution reactions [14], hydrogenation and hydrosilylation processes [15,16], cycloisomerization reactions [17], and the formation of C–C and C–heteroatom bonds [18]. Despite these advances, the integration of iron-supported zirconia systems into multicomponent reaction protocols remains comparatively underdeveloped, presenting an opportunity for further exploration.

In addition to transition metals, alkaline earth metals have attracted attention as environmentally benign catalytic alternatives. Magnesium chloride has been utilized effectively in aldol-type transformations [19], while chlorides of magnesium, calcium, barium, and strontium have shown efficiency in Biginelli condensations under green conditions [20]. Furthermore, calcium-based catalytic systems have been reported for the synthesis of various heterocyclic derivatives in aqueous media [21]. Due to their widespread natural abundance and lower toxicity compared with many transition metals, alkaline earth metals represent promising candidates for sustainable catalytic design [22,23]. Nevertheless, their broader application in multicomponent synthesis remains insufficiently explored.

This review aims to comprehensively summarize recent progress in zirconia-supported and earth-abundant metal-based catalytic systems applied in multicomponent reactions, with particular emphasis on green reaction conditions, catalyst recyclability, mechanistic insights, and synthetic scope. Furthermore, the challenges and future perspectives in designing efficient and sustainable catalytic systems for heterocyclic synthesis are discussed to provide direction for continued advancement in this field.

Synthetic Methodologies for the Construction of Polyhydroquinoline

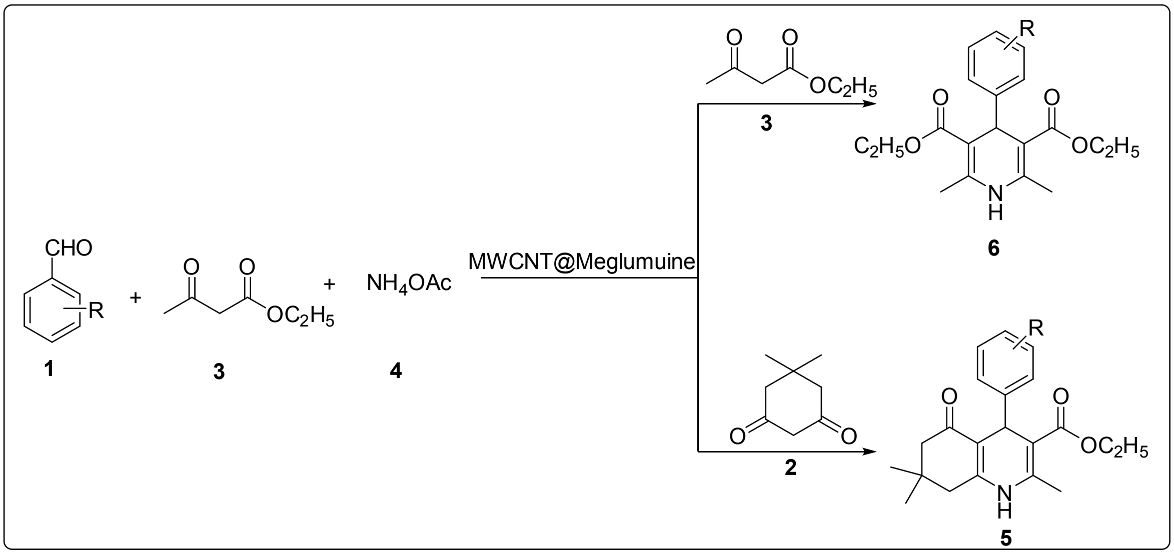
Z. Dehghanizadeh *et al.* [24] demonstrated an efficient synthesis of polyhydroquinoline derivatives through a multicomponent Hantzsch reaction involving aromatic aldehydes, dimedone, ethyl acetoacetate, and ammonium acetate under solvent-free conditions at 110 °C. The reaction was catalyzed by zinc oxide nanoparticles, which served as a green and effective Lewis acid. This approach offered several notable advantages, including high product yields, short reaction times, a clean reaction profile with minimal by-product formation, and a simple work-up procedure without the use of organic solvents. The study highlighted the potential of ZnO nanocatalysts in promoting environmentally benign transformations, aligning well with the principles of green chemistry for the synthesis of 1,4-dihydropyridines and polyhydroquinoline frameworks.



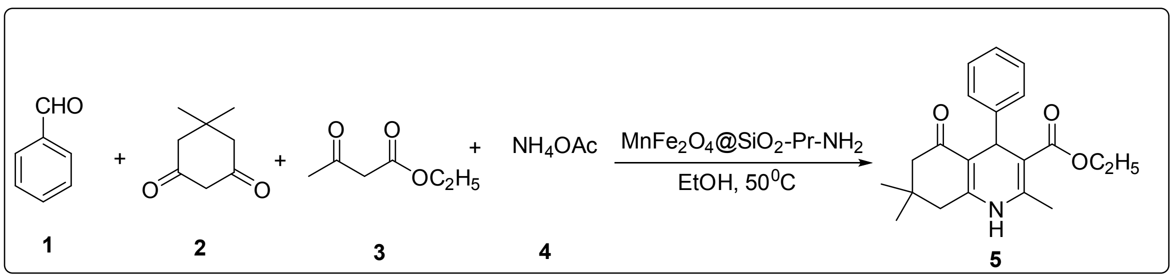
R. Mahinpour et al. [25] developed an efficient one-pot synthesis of 1,4-dihydropyridine derivatives via multicomponent condensation of aldehydes, ammonium acetate, and either dimedone or ethyl acetoacetate, using aminated multiwalled carbon nanotubes (MWCNTs) as a solid base catalyst. The catalyst, prepared through a simple and eco-friendly method, was employed in very small amounts (0.001 g) under thermal conditions, yielding products in good to excellent yields. The approach is notable for its simplicity, high efficiency, easy work-up, and reusability of the

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 8, April 2026 Impact Factor: 8.2

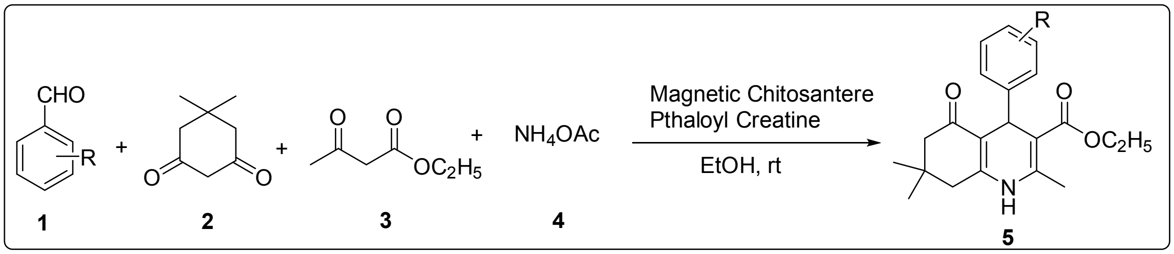
catalyst. In addition, antimicrobial screening revealed that most synthesized compounds exhibited activity against gram-positive bacteria, with select derivatives also showing antifungal properties.



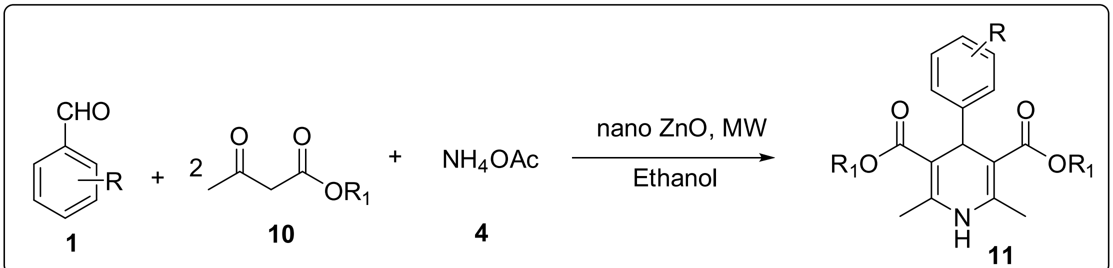
N. Ahadi *et al.* [26] reported the development of a novel heterogeneous catalyst by functionalizing manganese ferrite nanoparticles, encapsulated within a silica shell, with a Schiff base followed by copper incorporation. Comprehensive characterization of the hybrid catalyst was conducted using techniques such as FT-IR, XRD, FE-SEM, TEM, EDX, TGA, VSM, and ICP-OES. This organic–inorganic nanocatalyst demonstrated high efficiency and reusability in the green synthesis of 1,4-dihydropyridines and N-arylquinolines under mild reaction conditions. The products were obtained in good to excellent yields and characterized by FT-IR, ^{1}H NMR, and elemental analysis. Recyclability studies showed the catalyst maintained its performance over five consecutive runs with minimal copper leaching and only slight loss in catalytic activity.



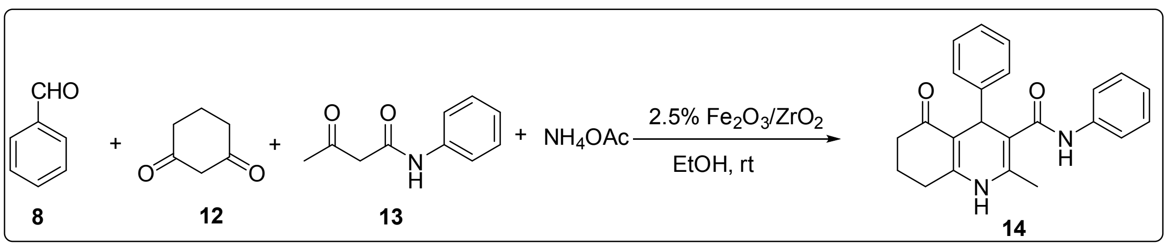
S. Asgharnasl *et al.* [27] developed a novel magnetic chitosan-terephthaloyl-creatine bionanocomposite, which was synthesized by functionalizing chitosan with creatine-terephthaloyl chloride ligands and magnetizing the substrate with Fe_3O_4 magnetic nanoparticles. The bionanocomposite was thoroughly characterized using FT-IR, EDX, FE-SEM, TEM, XRD, TGA, and VSM, revealing key structural features, including a magnetic saturation value of 92.96 emu/g and uniform nanoparticle size (~25-30 nm). This bionanocomposite was tested as a catalyst in the one-pot synthesis of polyhydroquinolines, 1,4-dihydropyridines, and 1,8-dioxo-decahydroacridine derivatives, achieving high yields and short reaction times under green chemistry principles. The catalyst's eco-friendly nature, excellent reusability, and efficiency highlight its potential for sustainable organic synthesis.



T. Ramanaik *et al.* [28] developed a novel approach was introduced for the synthesis of 1,4-dihydropyridine (1,4-DHP) derivatives, compounds known for their potential anti-cancer activity. The methodology employed a one-pot, multicomponent condensation reaction involving substituted benzaldehydes, acetylacetone, and ammonium acetate. Zinc nanoparticles (Zn NPs) as a catalyst significantly enhanced the reaction efficiency. Under the optimized conditions, the reaction reached completion in just few minutes, resulting in the formation of the target 1,4-DHP derivatives with an excellent yield of approximately 90%. This efficient synthetic protocol not only demonstrates the usefulness of Zn nanoparticles in promoting rapid and high-yielding reactions but also highlights the potential of microwave-assisted organic synthesis in medicinal chemistry, especially for the development of compounds with pharmacological importance like anti-cancer agents.

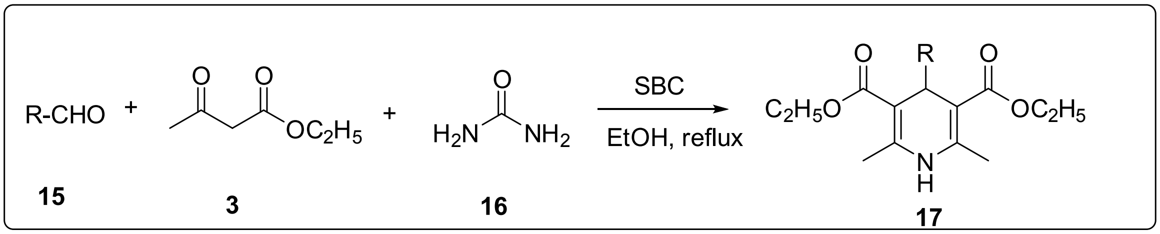


S.V.H.S. Bhaskaruni *et al.* [29] reported an innovative catalytic pathway for the synthesis of fused 1,4-dihydropyridine (1,4-DHP) derivatives. This method utilizes a multi-component condensation reaction involving cyclohexane-1,3-dione, benzaldehyde, ammonium acetate, and 3-oxo-N-phenylbutanamide. The reaction proceeds in ethanol at room temperature, with Fe_2O_3/ZrO_2 acting as an efficient heterogeneous catalyst. The use of the Fe_2O_3/ZrO_2 catalyst significantly enhances the reaction efficiency, enabling the formation of the fused 1,4-DHP products under mild conditions without the need for elevated temperatures or harsh reagents. Remarkably, this protocol achieves a high product yield, reaching up to 98%, demonstrating both the effectiveness and practicality of this catalytic system.

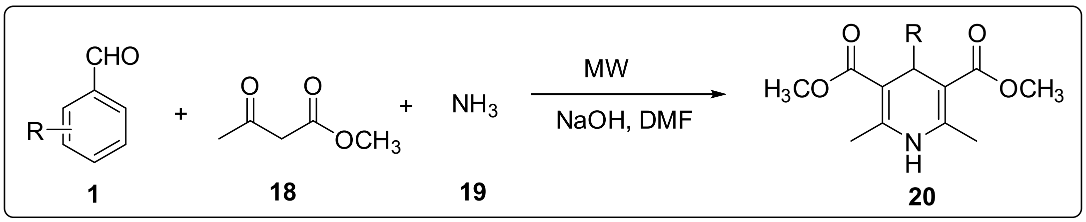


M. Ersatır *et al.* [30] reported a green and efficient method for synthesizing 1,4-dihydropyridines via a one-pot reaction of aromatic aldehydes, ethyl acetoacetate, and urea in sub-critical ethanol. This solvent system enabled high yields, short reaction times, and easy product isolation without additional catalysts. The mechanism involves ammonia generation and a Knoevenagel-type condensation. Although tested on only two heteroaromatic aldehydes, the method showed promising results and potential for broader application. GC-MS analysis also detected minor aromatized side products.

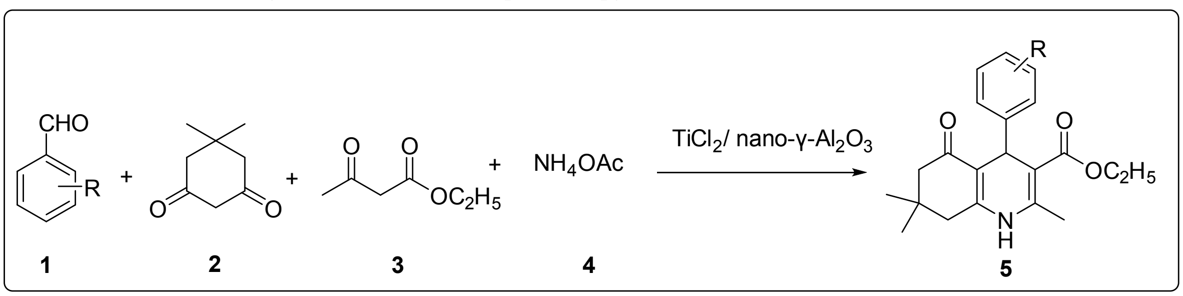
IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 8, April 2026 Impact Factor: 8.2



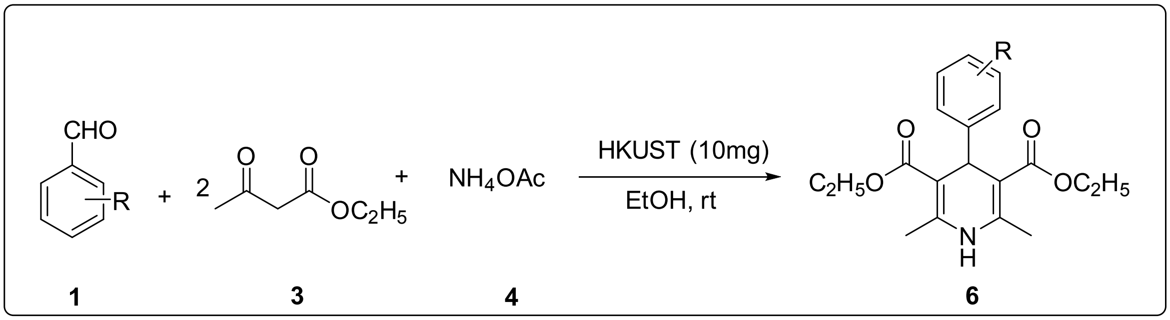
N. Kerru *et al.* [31] developed a green, catalyst-free method for synthesizing 1,2,4-triazole-tagged 1,4-dihydropyridine derivatives via a one-pot, four-component reaction involving 3-amino-1,2,4-triazole, diethyl acetylenedicarboxylate, malononitrile, and various aldehydes in water under microwave irradiation. This protocol delivered excellent yields (94–97%) within 12 minutes at room temperature, with no need for column chromatography. Structural confirmation was achieved through HRMS, ^{1}H NMR and ^{13}C NMR. The method is notable for its simplicity, eco-friendliness, rapidity, and broad functional group tolerance.



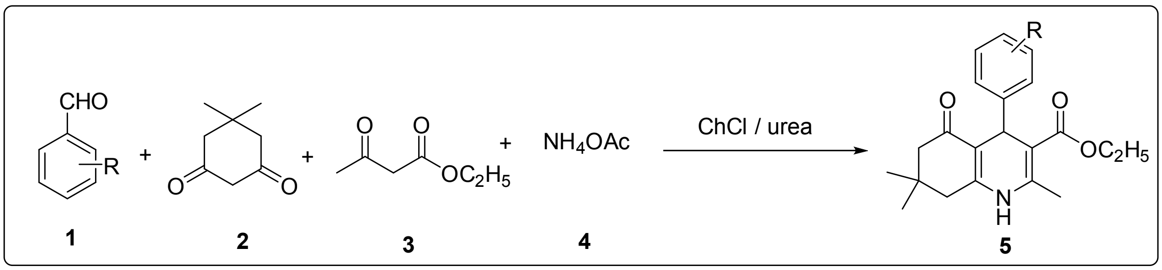
B. F. Mirjalili *et al.* [32] developed a green heterogeneous catalyst, $TiCl_2$/nano-γ-Al_2O_3, by immobilizing $TiCl_2$ onto nano-sized γ-alumina. The catalyst was characterized using standard techniques (FT-IR, XRD, FE-SEM, EDX, XRF, BET, and TGA) to confirm its structure and stability. Owing to their cost-efficiency, high activity, and recyclability, nano-catalysts have become increasingly valuable in organic synthesis. The catalytic efficiency of $TiCl_2$/nano-γ-Al_2O_3 was demonstrated in the solvent-free, multi-component synthesis of 1,4-dihydropyridine derivatives from aldehydes, 1,3-dicarbonyl compounds, dimedone and ammonium acetate, affording excellent yields in a short time. Product structures were confirmed by FT-IR and ^{1}H NMR spectroscopy.



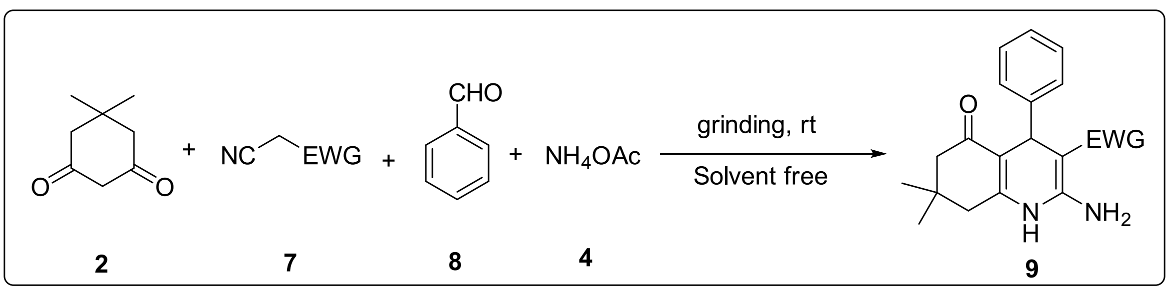
Z. Arzehgar et al. [33] introduced an efficient and straightforward protocol for the synthesis of Hantzsch 1,4-dihydropyridines using HKUST-1, a metal-organic framework, as a reusable solid catalyst. This solvent-free, one-pot approach was noted for its mild reaction conditions, short reaction times, and high product yields, even with minimal catalyst loading. Key advantages of this method include ease of catalyst preparation and handling, straightforward work-up, and the catalyst's recyclability, making it an attractive strategy for green synthesis of 1,4-DHP derivatives.



S. Pednekar *et al.* [34] developed an environmentally friendly and efficient protocol for the synthesis of structurally diverse 1,4-dihydropyridine derivatives using deep eutectic solvents (DESs) under solvent-free conditions. This one-pot multicomponent strategy not only delivered excellent yields but also highlighted the green potential of DESs (ChCl/urea) as biocompatible and recyclable media. Recyclability studies confirmed that the DES retained its catalytic activity with minimal efficiency loss over five consecutive reaction cycles. The method stands out due to its operational simplicity, mild reaction conditions, and minimal environmental impact, offering a sustainable alternative to conventional synthetic approaches for 1,4-DHP compounds.



S. Kumar et al. [35] reported a solvent-free, catalyst-free protocol for the synthesis of polyhydroquinoline derivatives via a four-component Hantzsch condensation involving aldehydes, dimedone, active methylene compounds, and ammonium acetate. The reaction was carried out under ambient conditions by simple grinding of the reactants, eliminating the need for hazardous organic solvents or complex purification steps. Products were isolated in high yields with short reaction times and purified through straightforward recrystallization using ethanol, avoiding chromatographic techniques. This method is notable for its operational simplicity, eco-friendliness, tolerance to a wide range of functional groups, and overall efficiency, making it a valuable approach for the green synthesis of polyhydroquinolines.



2. Conclusion

Polyhydroquinolines remain a highly significant class of heterocyclic compounds owing to their broad pharmacological relevance and structural versatility. Considerable progress has been achieved in their synthesis through multicomponent strategies, particularly Hantzsch-type reactions, which offer operational simplicity, high atom economy, and structural diversity. The shift toward sustainable methodologies, employing recyclable heterogeneous catalysts, earth-abundant metals, green solvents, and energy-efficient activation techniques has substantially enhanced the environmental compatibility of these processes.

Despite these advances, further efforts are required to improve catalyst robustness, expand substrate scope, and ensure scalability for practical applications. Continued innovation in green catalytic design is expected to further streamline the synthesis of polyhydroquinoline derivatives and strengthen their accessibility for pharmaceutical and industrial development.

REFERENCES

[1]. B.H. Rotstein, S. Zaretsky, V. Rai, A.K. Yudin, Chem. Rev., 114, 8323 (2014).
[2]. A Dömling, W. Wang, K. Wang, Chem. Rev., 112, 3083 (2012).
[3]. S.V.H.S. Bhaskaruni, S. Maddila, K.K. Gangu, S.B. Jonnalagadda, Arab. J. Chem., (2017).
[4]. R.A. Sheldon, Chem. Soc. Rev., 41, 1437 (2012).
[5]. R. Pagadala, S. Maddila, S. Rana, S.B. Jonnalagadda, RSC Adv., 4, 6602 (2014).
[6]. C.J. Védrine, Catal., 7, 341 (2017).
[7]. V. Menon, V. Popa, C. Contescu, J.A. Schwarz, Rev. Roum. Chim., 43, 393 (1998).
[8]. S. Kouva, K. Honkala, L. Leferts, J. Kanervo, Catal. Sci. Technol., 5, 3473 (2015).
[9]. Y. Zhao, W. Li, M. Zhang, K. Tao, Catal. Commun., 3, 239 (2002).
[10]. V. Kozell, T. Giannoni, M. Nocchetti, R. Vivani, O. Piermatti, L. Vaccaro, Catal., 7, 186 (2017).
[11]. M. Sharbatdaran, F. Farzaneh, M.M. Larijani, J. Mol. Catal. A Chem., 382, 79 (2014).
[12]. M.B. Gawande, R.K. Pandey, R.V. Jayaram, Catal. Sci. Technol., 2, 1113 (2012).
[13]. Bauer, H.-J. Knölker, Chem. Rev., 115, 3170 (2015).
[14]. B. Åkermark, M.P.T. Sjögren, Adv. Synth. Catal., 349, 2641 (2007).
[15]. R.N. Naumov, M. Itazaki, M. Kamitani, H. Nakazawa, J. Am. Chem. Soc., 134, 804 (2012).
[16]. N.S. Shaikh, K. Junge, M. Beller, Org. Lett., 9, 5429 (2007).
[17]. A Guðmundsson, K.P.J. Gustafson, B.K. Mai, B. Yang, F. Himo, J.-E. Bäckvall, ACS Catal., 8, 12 (2018).
[18]. B Cassani, G. Bergonzini, C.-J. Wallentin, ACS Catal., 6, 1640 (2016).
[19]. K. Miura, T. Nakagawa, A. Hosomi, Synlett, 12, 1917 (2015).
[20]. K. Shahnaz, M.H. Majid, M. Kargar, F.K.B. Zohreh, Green Chem., 1, 133 (2008).
[21]. S. Yaragorla, G. Singh, A. Pareek, Indian J. Chem., 54, 1321 (2015).
[22]. S. Kobayashi, Y. Yamashita, Acc. Chem. Res., 44, 58 (2011).
[23]. J.S. Alexander, K. Ruhlandt-Senge, Eur. J. Inorg. Chem., 11, 2761 (2002).
[24]. Z. Dehghanizadeh, F. Buazar, J. Heterocycl. Chem., 8, 18 (2018).
[25]. L. Moradi, R. Mahinpour, Z. Zahraei, N. Pahlevanzadeh, J. Saudi Chem. Soc., 22, 876 (2018).
[26]. N. Ahadi, A. Mobinikhaledi, M.A. Bodaghifard, Appl. Organomet. Chem., 34, 18 (2020).
[27]. S. Asgharnasl, R. Eivazzadeh-Keihan, F. Radinekiyan, A. Maleki, Int. J. Biol. Macromol., 144, 29 (2020).
[28]. T. Ramanaik, R. Naik, Org. Synth., 1, (2020).
[29]. S.V.H.S. Bhaskaruni, S. Maddila, W.E. van Zyl, S.B. Jonnalagadda, Res. Chem. Intermed., 45, 4555 (2019).
[30]. M. Erşatır, M. Türk, E.S. Giray, J. Supercrit. Fluids, 176, 105303 (2021).
[31]. N. Kerru, S. Maddila, S.B. Jonnalagadda, Front. Chem., 9, 638832 (2021).
[32]. B.F. Mirjalili, A. Bamoniri, L. Asadollah Salmanpoor, J. Nanostruct., 8, 276 (2018).
[33]. Z. Arzehgar, S. Sajjadifar, H. Arandiyan, Asian J. Green Chem., 3, 43 (2019).
[34]. S. Pednekar, R. Bhalerao, N. Ghadge, Chem. Sci. J., 125, 615 (2013).
[35]. S. Kumar, P. Sharma, K.K. Kapoor, M.S. Hundal, Tetrahedron, 64, 536 (2008).