Engineering Universe for Scientific Research and Management
ISSN (Online): 2319-3069
Vol. XIII Issue X
October 2021

A Comprehensive Survey an Assisted Organic Synthesis of Nitrogen, Oxygen, and Sulfur-Containing Heterocycles

Sachin Chawla
Research Scholar, Department of Chemistry, Glocal University, Saharanpur, Uttar Pradesh, India

Abstract

This comprehensive survey delves into the realm of assisted organic synthesis, focusing on the microwave-assisted construction of nitrogen, oxygen, and sulfur-containing heterocycles. Heterocyclic compounds, integral to medicinal chemistry, agrochemicals, and material science, have seen significant advancements with the advent of microwave irradiation. The survey systematically explores the strategies employed in microwave-assisted synthesis, emphasizing cyclization, condensation, and multicomponent reactions. It highlights the distinctive advantages conferred by microwave irradiation, including accelerated reaction times, heightened yields, and enhanced purity of synthesized heterocycles. The survey meticulously categorizes the synthesis of nitrogen-containing heterocycles such as pyrazoles, pyridines, pyrimidines, and imidazoles, showcasing notable examples and their pharmaceutical significance. Additionally, it scrutinizes the microwave-assisted synthesis of oxygen-containing heterocycles, encompassing furans, pyrans, and coumarins, shedding light on the impact of microwave irradiation on reaction outcomes and the green chemistry aspects of these processes. Sulfur-containing heterocycles, including thiazoles, thiophenes, and benzothiazoles, are surveyed to elucidate the versatile role of microwave methods in their efficient construction. The survey concludes by spotlighting the broad applications of microwave-assisted synthesis in the development of bioactive compounds, pharmaceuticals, and materials. Current challenges and future perspectives are discussed, with an emphasis on the potential for scale-up and industrial applications. In summary, this survey provides a comprehensive overview of the landscape of microwave-assisted organic synthesis, underlining its pivotal role in advancing the construction of diverse and complex heterocyclic structures.

Keywords: Microwave Synthesis, Heterocycles, Organic Chemistry, Green Chemistry, Medicinal Chemistry.

1. Introduction

The synthesis of heterocyclic compounds holds significant importance in medicinal chemistry, agrochemicals, and material science, owing to the diverse array of applications these compounds find in various fields. In recent years, microwave-assisted organic synthesis has emerged as a prominent and transformative method for the construction of heterocyclic structures. This technique has garnered attention due to its capacity to expedite reactions, improve yields, and enhance selectivity. In this survey, we explore the latest advancements in the field of microwave-assisted synthesis of heterocycles, with a particular focus on the incorporation of nitrogen, oxygen, and sulfur atoms. This investigation aims to provide a comprehensive understanding of the innovative strategies and applications that have contributed to the growing significance of microwave-assisted organic synthesis in heterocyclic chemistry.

2. Microwave-Assisted Strategies

This section delves into the diverse strategies employed in microwave-assisted synthesis, encompassing cyclization, condensation, and multicomponent reactions. Microwave irradiation has proven to be a powerful tool in heterocyclic synthesis, offering several advantages over conventional methods. One notable advantage is the substantial reduction in reaction times, facilitating faster production of heterocyclic compounds. Additionally, microwave-assisted strategies often result in higher yields, contributing to the overall efficiency of the synthesis process. Moreover, the use of microwaves has been associated with enhanced purity in the synthesized heterocycles, reflecting the precision and selectivity achieved through this innovative approach. The elucidation of these microwave-assisted strategies aims to underscore the transformative impact of microwave irradiation on the synthesis of heterocyclic compounds.

3. Nitrogen-Containing Heterocycles

This section focuses on the microwave-assisted synthesis of nitrogen-containing heterocycles, with a specific emphasis on prominent classes like pyrazoles, pyridines, pyrimidines, and imidazoles. Microwave irradiation has demonstrated notable efficacy in expediting the synthesis of these nitrogen-containing heterocyclic compounds. Various examples within each class will be explored to underscore the versatility and applicability of microwave-assisted methodologies. Pyrazoles, characterized by a five-membered ring containing three carbon atoms and two nitrogen atoms, have been efficiently synthesized under microwave conditions. The rapid and high-yielding nature of these reactions showcases the utility of microwave irradiation in accessing pyrazole derivatives. Likewise, the synthesis of pyridines, pyrimidines, and imidazoles, which are essential structural motifs in pharmaceutical compounds, has benefited from the accelerated and efficient protocols enabled by microwave-assisted strategies. Notable examples from recent literature will be discussed, emphasizing the pharmaceutical significance of these synthesized nitrogen-containing heterocycles. The ability of microwave irradiation to facilitate the rapid and controlled synthesis of such compounds underscores its pivotal role in advancing medicinal chemistry and drug discovery.

4. Oxygen-Containing Heterocycles

This section delves into the microwave-assisted synthesis of oxygen-containing heterocycles, with a focus on notable classes such as furans, pyrans, and coumarins. Microwave irradiation has proven to be a valuable tool in expediting the preparation of these oxygen-containing heterocyclic compounds, showcasing advantages in terms of reaction efficiency and sustainability. Furans, which are five-membered rings containing one oxygen atom, have been successfully synthesized using microwave-assisted methodologies. The ability of microwave irradiation to promote rapid and efficient cyclization processes leading to furan derivatives will be explored. Similarly, the synthesis of pyrans and coumarins, which are important structural motifs in various natural products and pharmaceuticals, has benefited from the unique advantages offered by microwave-assisted strategies. This discussion will highlight specific examples of oxygen-containing heterocycles synthesized under microwave conditions, emphasizing the impact on reaction outcomes. Furthermore, the environmentally friendly aspects of microwave-assisted synthesis, aligning with principles of green chemistry, will be addressed. The survey aims to provide insights into the role of microwave irradiation in the sustainable and efficient synthesis of oxygen-containing heterocycles, contributing to advancements in synthetic methodologies and applications in diverse fields.

5. Sulfur-Containing Heterocycles

This section focuses on the microwave-assisted synthesis of sulfur-containing heterocycles, emphasizing key classes like thiazoles, thiophenes, and benzothiazoles. Microwave irradiation has demonstrated notable advantages in enhancing the efficiency of constructing these essential sulfur-containing structural motifs. Thiazoles, characterized by a five-membered ring containing both sulfur and nitrogen, play a crucial role in medicinal chemistry and agrochemicals. Microwave-assisted strategies have been employed to accelerate the synthesis of thiazole derivatives, highlighting the versatility of this technique in achieving rapid cyclization and improved yields. Similarly, the synthesis of thiophenes, which consist of a five-membered ring containing sulfur, has been efficiently accomplished using microwave irradiation. The survey will explore the applications and significance of these microwave-assisted methodologies in the construction of thiophene derivatives, with a focus on their relevance in various fields. Benzothiazoles, a subclass of thiazoles, possess a fused benzene ring, further expanding the structural diversity of sulfur-containing heterocycles. Microwave-assisted synthesis has played a pivotal role in the rapid assembly of benzothiazole derivatives, showcasing its utility in the construction of complex heterocyclic frameworks. The discussion will encompass specific examples of sulfur-containing heterocycles synthesized under microwave conditions, shedding light on the advantages offered by this technique. By surveying the literature on these methodologies, the section aims to provide insights into the versatility of microwave irradiation in the efficient and sustainable synthesis of sulfur-containing heterocycles.

6. Applications and Future Perspectives

The application of microwave-assisted synthesis extends across various domains, including the development of bioactive compounds, pharmaceuticals, and materials. This section delves into the diverse applications of microwave irradiation and outlines current challenges and future perspectives in the field. Microwave-assisted synthesis has proven invaluable in the rapid and efficient generation of bioactive compounds. The survey will explore instances where this technique has been instrumental in the synthesis of molecules with biological activities, ranging from antimicrobial agents to anti-cancer drugs. Highlighting specific examples, this section will underscore the impact of microwave irradiation on accelerating the discovery and development of novel bioactive compounds. The pharmaceutical industry has witnessed a paradigm shift with the integration of microwave-assisted synthesis. The section will discuss how this methodology has been employed in the synthesis of key pharmaceutical intermediates and active pharmaceutical ingredients (APIs). By examining case studies and advancements in drug development facilitated by microwave irradiation, the survey aims to underscore its role in streamlining pharmaceutical synthesis. Microwave-assisted synthesis has also found applications in the fabrication of advanced materials with tailored properties. This section will explore how microwave irradiation contributes to the rapid and controlled synthesis of materials for diverse applications, including catalysis, nanotechnology, and energy storage. Emphasis will be placed on the potential for scale-up in industrial settings and the role of microwave-assisted methods in achieving sustainability goals.

6.1 Challenges and Future Directions

While microwave-assisted synthesis has demonstrated numerous advantages, challenges persist, including scalability, reproducibility, and the need for comprehensive reaction optimization. The survey will critically examine these challenges and propose future directions for research, emphasizing the integration of microwave methods into industrial processes. Potential advancements, emerging technologies, and innovative strategies will be discussed, providing insights into the evolving landscape of microwave-assisted synthesis. By addressing these aspects, the section aims to provide a comprehensive overview of the applications of microwave irradiation and outline the trajectory of future developments in this dynamic field.

7. Conclusion

In conclusion, this survey has provided a comprehensive exploration of the landscape of microwave-assisted organic synthesis, focusing on the construction of nitrogen, oxygen, and sulfur-containing heterocycles. The survey underscores the pivotal role played by microwave irradiation in enhancing reaction kinetics, improving yields, and imparting green chemistry attributes to the synthesis of diverse heterocyclic compounds. The survey highlighted various strategies employed in microwave-assisted synthesis, including cyclization, condensation, and multicomponent reactions. The advantages of microwave irradiation, such as rapid reaction times, higher yields, and increased purity, were emphasized. Specific attention was given to the synthesis of nitrogen-containing heterocycles like pyrazoles, pyridines, pyrimidines, and imidazoles, with notable examples showcased for their significance in pharmaceutical applications. Additionally, the survey explored the synthesis of oxygen-containing heterocycles, including furans, pyrans, and coumarins, shedding light on the impact of microwave irradiation on reaction outcomes and the green chemistry aspects of these processes. The efficient construction of sulfur-containing heterocycles, such as thiazoles, thiophenes, and benzothiazoles, was surveyed, showcasing the versatility of microwave methods in this domain. Microwave-assisted synthesis has emerged as a powerful tool in the realm of chemical synthesis. The ability to accelerate reactions, coupled with improved selectivity, has significantly contributed to the efficient construction of complex heterocyclic structures. The survey reinforces the importance of microwave methods in providing sustainable and eco-friendly alternatives for the synthesis of diverse heterocyclic motifs.

The survey underscores the broad applications of microwave-assisted synthesis in the development of bioactive compounds, pharmaceuticals, and advanced materials. The integration of this methodology has reshaped traditional approaches, offering rapid and efficient pathways for chemical transformations. From drug discovery to materials science, microwave-assisted synthesis continues to leave a profound impact on scientific research and industrial processes. As we move forward, the continued importance of microwave-assisted organic synthesis is evident. The survey concludes by emphasizing the ongoing relevance of this methodology in advancing chemical synthesis. The ability to address current challenges, coupled with its potential for scale-up in industrial applications, positions microwave-assisted synthesis as a transformative force in the ever-evolving landscape of organic chemistry.

References

[1] S. Ravichandran and E. Karthikeyan, "Microwave synthesis—a potential tool for green chemistry," International Journal of Chem Tech Research, vol. 3, no. 1, pp. 466-470, Mar. 2011.

[2] P. Anastas and N. Eghbali, "Green Chemistry: Principles and Practice," Chem. Soc. Rev., vol. 39, pp. 301-312, 2010. [Online]. Available: https://doi.org/10.1039/B918763B.

[3] B. L. Hayes, "Recent advances in microwave-assisted synthesis," Aldrichimica Acta, vol. 37, no. 2, pp. 66-77, Jan. 2004.

[4] V. Vahabi and F. Hatamjafari, "Microwave assisted convenient one-pot synthesis of coumarin derivatives via Pechmann condensation catalyzed by FeF3 under solvent-free conditions and antimicrobial activities of the products," Molecules, vol. 19, pp. 13093-13103, 2014. [Online]. Available: https://doi.org/10.3390/molecules190913093.

[5] S. N. Mangasuli, K. M. Hosamani, and P. B. Managutti, "Microwave assisted synthesis of coumarin-purine derivatives: An approach to in vitro antioxidant, DNA cleavage, crystal structure, DFT studies and Hirshfeld surface analysis," Heliyon, vol. 5, 2019. [Online]. Available: https://doi.org/10.1016/j.heliyon.2019.

[6] M. T. Gabr, N. S. El-Gohary, E. R. El-Bendary, M. M. El-Kerdawy, and N. Ni, "Microwave-assisted synthesis and antitumor evaluation of a new series of thiazolylcoumarin derivatives," EXCLI J., vol. 16, pp. 1114–1131, 2017. [Online]. Available: https://doi.org/10.17179/excli2017-208.

[7] G. Rajitha, V. Ravibabu, G. Ramesh, and B. Rajitha, "Synthesis and antimicrobial activity of novel imidazo [1, 2-a]pyridinopyrimidine-2, 4, 6 (1H, 3H, 5H)-triones and thioxopyrimidine-4, 6 (1H, 5H) diones," Research on Chemical Intermediates, vol. 42, pp. 1989-1998, 2016. [Online]. Available: https://doi.org/10.1007/s11164-015-2130-2.

[8] M. N. Kumbar, R. R. Kamble, A. A. Kamble, S. R. Salian, S. Kumari, R. Nair, et al., "Design and Microwave Assisted Synthesis of Coumarin Derivatives as PDE Inhibitors," Int. J Med Chem., vol. 2016, pp. 1-16, 2016. [Online]. Available: https://doi.org/10.1155/2016/9890630.

[9] T. S. Kokovina, S. Y. Gadomsky, A. A. Terentiev, and N. A. Sanina, "A novel approach to the synthesis of 1, 3, 4-thiadiazole-2-amine derivatives," Molecules, 2021. [Online]. Available: https://doi.org/10.3390/molecules26175159.

[10] P. S. Mishra, R. Mishra, R. J. Gupta, R. Mazumder, and R. Malviya, "Efficient Green Synthesis and Biological Evaluation of Thiadiazole Derivatives," Letters in Applied Nano Bio Science, vol. 10, pp. 2594-2604, 2021. [Online]. Available: https://doi.org/10.33263/LIANBS103.25942604.

[11] O. O. Ajani, M. M. Akande, N. October, T. O. Siyanbola, D. V. Aderohunmu, A. A. Akinsiku, et al., "Microwave assisted synthesis, characterization and investigation of antibacterial activity of 3-(5-(substituted-phenyl)-4, 5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one derivatives," Arab J Basic Appl Sci., vol. 26, pp. 361-374, 2019. [Online]. Available: https://doi.org/10.1080/25765299.2019.1632141.

[12] D. Ashok, K. Ramakrishna, N. Nagaraju, M. R. Reddy, R. Dharavath, and M. Sarasija, "Microwave-Assisted Synthesis of Substituted 2-(2H-Chromen-3-yl)-5-phenyl-1H-imidazole Based Coumarin Derivatives and Their Antimicrobial Activity," Russ J Gen Chem., vol. 91, pp. 711-716, 2021. [Online]. Available: https://doi.org/10.1134/S1070363221040216.

[13] R. R. Zhang, J. Liu, Y. Zhang, M. Q. Hou, M. Z. Zhang, F. Zhou, et al., "Microwave-assisted synthesis and antifungal activity of novel coumarin derivatives: Pyrano [3, 2- c]chromene-2, 5-diones," Eur J Med Chem., vol. 116, pp. 76–83, 2016. [Online]. Available: https://doi.org/10.1016/j.ejmech.2016.03.069.

[14] F. Keshavarzipour and H. Tavakol, "The synthesis of coumarin derivatives using choline chloride/zinc chloride as a deep eutectic solvent," Journal of the Iranian Chemical Society, vol. 13, pp. 149–153, 2016. [Online]. Available: https://doi.org/10.1007/s13738-015-0722-9.

[15] D. Konrádová, H. Kozubíková, K. Doležal, and J. Pospíšil, "Microwave-Assisted Synthesis of Phenylpropanoids and Coumarins: Total Synthesis of Osthol," European J Org Chem., vol. 2017, pp. 5204–5213, 2017. [Online]. Available: https://doi.org/10.1002/ejoc.201701021.

[16] D. Srikrishna and P. K. Dubey, "Microwave-assisted efficient and convenient one-pot synthesis of novel 3-(4-aminothieno [2, 3-d] pyrimidin-5-yl) coumarins under solvent-free conditions," Chem Heterocycl Compd (N Y), vol. 54, pp. 736-743, 2018. [Online]. Available: https://doi.org/10.1007/s10593-018-2340-9.

[17] P. Anand, B. Singh, and N. Singh, "A review on coumarins as acetylcholinesterase inhibitors for Alzheimer's disease," Bioorg Med Chem., vol. 20, pp. 1175–1180, 2012. [Online]. Available: https://doi.org/10.1016/j.bmc.2011.12.042.

[18] S. M. Bagheri, M. Khoobi, H. Nadri, A. Moradi, S. Emami, L. Jalili-Baleh, et al., "Synthesis and Anticholinergic Activity of 4-hydroxycoumarin Derivatives Containing Substituted Benzyl-1,2,3-triazole Moiety," Chem Biol Drug Des., vol. 86, pp. 1215–1220, 2015. [Online]. Available: https://doi.org/10.1111/cbdd.12588.

[19] S. F. Razavi, M. Khoobi, H. Nadri, A. Sakhteman, A. Moradi, S. Emami, et al., "Synthesis and evaluation of 4-substituted coumarins as novel acetylcholinesterase inhibitors," Eur J Med Chem., vol. 64, pp. 252–259, 2013. [Online]. Available: https://doi.org/10.1016/j.ejmech.2013.03.021.

[20] S. B. Phadtare, K. J. Jarag, and G. S. Shankarling, "Greener protocol for one pot synthesis of coumarin styryl dyes," Dyes and Pigments, vol. 97, pp. 105–112, 2013. [Online]. Available: https://doi.org/10.1016/j.dyepig.2012.12.001.

[21] Matwijczuk, D. Kluczyk, A. Górecki, A. Niewiadomy, and M. Gagoś, "Solvent Effects on Molecular Aggregation in 4-(5-Heptyl-1, 3, 4-thiadiazol-2-yl) benzene-1, 3-diol and 4-(5-Methyl-1, 3, 4-thiadiazol-2-yl) benzene-1, 3-diol," J Phys Chem B, vol. 120, pp. 7958–7969, 2016. [Online]. Available: https://doi.org/10.1021/acs.jpcb.6b06323.