InSight Bulletin: A Multidisciplinary Interlink International Research Journal
Peer Reviewed International, Open Access Journal.
ISSN : 3065-7857 / Website: https://ibrj.us / Volume-2, Issue-12 / December - 2025

Original Article

Flow Chemistry Improvements and Industrial Applications

Sharad V. Sonawane[1], Dattatray A. Chadar[2]
[1,2] Sandip University, Trimbak Road, Mahiravani, Nashik. Maharashtra, India.

Manuscript ID:
IBMIIRJ -2025-021210

Submitted: 05 Nov. 2025

Revised: 10 Nov. 2025

Accepted: 06 Dec. 2025

Published: 31 Dec. 2025

ISSN: 3065-7857

Volume-2

Issue-12

Pp.40-45

December 2025

Correspondence Address:
Sharad V. Sonawane, Sandip University, Trimbak Road, Mahiravani, Nashik. Maharashtra, India.
Email: sharad612@gmail.com

Quick Response Code:

Web. https://ibrj.us

DOI: 10.5281/zenodo.18357948

DOI Link:
https://doi.org/10.5281/zenodo.18357948

Abstract

Flow chemistry has emerged as a transformative approach to chemical synthesis, offering substantial advantages over traditional batch methods. This review traces the development of continuous-flow processing and outlines the fundamental principles underlying its growing adoption across multiple sectors. Key innovations in reactor engineering, such as microstructured devices, modular systems, and integrated continuous platforms, have expanded the operational capabilities of flow systems, enabling precise reaction control, enhanced heat and mass transfer, and improved safety of chemical reactions. These technical advancements have accelerated the application of flow chemistry in pharmaceutical manufacturing, where continuous processing supports the efficient production of active pharmaceutical ingredients (API), rapid reaction screening, and streamlined scale-up. Beyond pharmaceuticals, flow technologies have facilitated progress in materials science, including the controlled synthesis of polymers, nanomaterials, and advanced functional materials. This method aligns with the goals of sustainable chemical manufacturing by reducing waste, improving energy efficiency, and enabling the safe handling of reactive intermediates. Despite these strengths, several challenges remain, including the need for improved process optimization strategies, greater automation, and seamless integration of multi-step synthetic sequences. Ongoing research on inline analytics, machine-assisted control, and fully continuous end-to-end workflows is expected to overcome these limitations in the future. As these developments continue to mature, flow chemistry is poised to play an increasingly central role in modern chemical production, providing faster, greener, and more reliable pathways for complex molecular synthesis.

Keywords: *Flow chemistry, Continuous processing, Reactor engineering, pharmaceutical manufacturing, Material synthesis, Sustainable chemical production.*

Introduction

Continuous-flow chemistry, often referred to as flow chemistry, is a modern technique in chemical synthesis that involves the steady movement of reactants through a reactor, where conditions such as temperature, pressure, and reaction time are controlled. In contrast to conventional batch processes, in which reactants are combined in a single container and allowed to react over time, flow systems offer dynamic control by adjusting the rate at which substances are introduced and processed (Wang et al. 2012). This level of precision enables the rapid optimization of reaction parameters and supports the efficient creation of structurally complex molecules with improved selectivity and performance (Baxendale et al., 2013). The growing interest in both research and industry is due to its advantages over traditional methods. The key strength of this method is its safety, as the reactions occur in small, controlled volumes (Hartman et al., 2011). Flow systems are highly adaptable, allowing the scale-up of production from small laboratory samples to larger industrial quantities (Kockmann et al., 2012). Flow chemistry benefits from superior heat and mass transfer, resulting in higher reaction yields, better product purity, and greater selectivity than batch processing (Jensen, 2019). The integration of automated systems and in-line analytical tools allows for real-time tracking and adjustment of reaction conditions, thereby streamlining the development and manufacture of pharmaceuticals and fine chemicals (Adamo et al., 2016).

Flow Chemistry Through the Decades: Milestones, Innovations & Impact

The foundations of flow chemistry were established in the 20th century by Prelog and Mislow (Wiles & Watts, 2012). Significant progress has been made in the 21st century to achieve these goals. In 2004, Wiles and Watts (2004).

How to cite this article:
Sonawane, S. V., & Chadar, D. A. (2025). Flow Chemistry Improvements and Industrial Applications. InSight Bulletin: A Multidisciplinary Interlink International Research Journal, 2(12), 40–45. https://doi.org/10.5281/zenodo.18357948

This was published in comprehensive reviews by Ley and Jensen in 2010, which helped in this direction (Ley et al., 2010; Jensen, 2010). Flow chemistry has evolved in response to the increasing demand for processes that are more efficient, scalable, and safe than traditional batch methods. Microreactor systems have played a crucial role in the development of sophisticated reactor types, such as continuous stirred tank reactors (CSTRs), plug flow reactors (PFRs), and oscillatory flow reactors (OFRs) (Wiles & Watts, 2012; Movsisyan et al., 2016).

In recent years, improvements in reactor design, construction materials, and integration with automation technologies have been significant. (Hessel et al., 2013; Porta et al., 2016). The research group led by Steven Ley at the University of Cambridge has made substantial advances in the use of flow systems for complex organic syntheses, introducing innovative methodologies in this process (Fors et al., 2012; Battilocchio & Ley, 2016). Moreover, Jensen's team at MIT focused on applying microreactor technology to pharmaceutical manufacturing processes. (Jensen et al., 2011; Adamo et al., 2013).

Principles of Flow Chemistry

Flow chemistry is a transformative approach to chemical synthesis that offers distinct advantages over traditional batch processing methods. Unlike batch reactions, which occur in a single, often large-volume vessel, flow chemistry involves the continuous movement of reactants through a reactor system. This significantly enhances the control over key reaction parameters, such as temperature, pressure, and residence time, thereby improving reaction efficiency and selectivity (Wiles & Watts, 2012; Hartman et al., 2011).

Various flow reactor designs have been developed to suit different chemical processes. The most commonly employed reactors are Continuous Stirred-Tank Reactors (CSTRs), Plug Flow Reactors (PFRs), and Oscillatory Flow Reactors (OFRs). Each design offers unique benefits depending on the reaction conditions and their kinetics. CSTRs are often used for rapid and homogeneous reactions because of their consistent mixing capabilities. PFRs are more appropriate for processes that benefit from longer residence times and plug-like flow characteristics, which lead to enhanced product uniformity. OFRs exhibit oscillatory motion, which improves mixing and heat transfer without requiring high flow rates, making them suitable for complex and highly exothermic reactions (Movsisyan et al., 2016; Wiles & Watts, 2012).

The high degree of control in flow systems allows for the streamlined optimization of reaction conditions, which is a fraction of the time required for batch processing. This is beneficial in multistep syntheses or reactions, where precision is critical for the yield and purity (Jensen, 2019). Moreover, the integration of online analytical techniques and process automation facilitates real-time data acquisition and parameter adjustment. These capabilities significantly enhance the reproducibility and process efficiency while enabling dynamic adaptation to changing reaction conditions (Adamo et al., 2016).

Emerging Developments in Flow Chemistry

Flow chemistry is increasingly employed for the production of active pharmaceutical ingredients (APIs) and synthetic intermediates, offering multiple advantages over conventional batch-processing methods. These include greater reaction selectivity, shorter processing times, and improved safety when handling hazardous and unstable reagents (Baxendale et al., 2016). One application is the continuous flow synthesis of artemisinin, an antimalarial drug (Koos et al., 2011). Flow chemistry is gaining traction in materials science. recise control over reaction variables, such as temperature, residence time, and reagent mixing, enables the production of advanced materials, nanoparticles, and polymers. (Kundu et al., 2018). An example is the continuous flow synthesis of metal-organic frameworks (MOFs), which demonstrates their applications in gas storage, catalysis, and drug delivery (Patterson et al., 2012). Flow chemistry aligns with the objectives of green chemistry, focusing on waste minimization and the use of sustainable resources. The inherent safety and efficiency of reactions involving highly reactive species are too dangerous or unstable for batch processing (Hone et al., 2019). Moreover, coupling flow systems with real-time analytical tools allows for in-line monitoring and optimization, reducing reaction waste and enhancing product yields (Pastre et al., 2013).

Table 1: Advantages and Disadvantages of Flow Chemistry

Aspect	Advantages	Disadvantages
Process Management	Allows for exact regulation of all chemical parameters and conditions.	Expertise is necessary for the proper design and practical operation of a continuous-flow reactor.
Scaling	Provides seamless scalability from small laboratory experiments up to full-scale industrial manufacturing.	Requires a substantial initial investment for equipment and system installation.
Operational Safety	Enhanced safety during operation, primarily due to integrated, automated control systems.	The complexity of the flow systems can make maintenance and troubleshooting more difficult.
Sustainability	Reduced environmental footprint through lower energy consumption and less chemical waste production.	Ensuring chemical compatibility between construction materials and reagents/solvents can be challenging.

Applications of Flow Chemistry

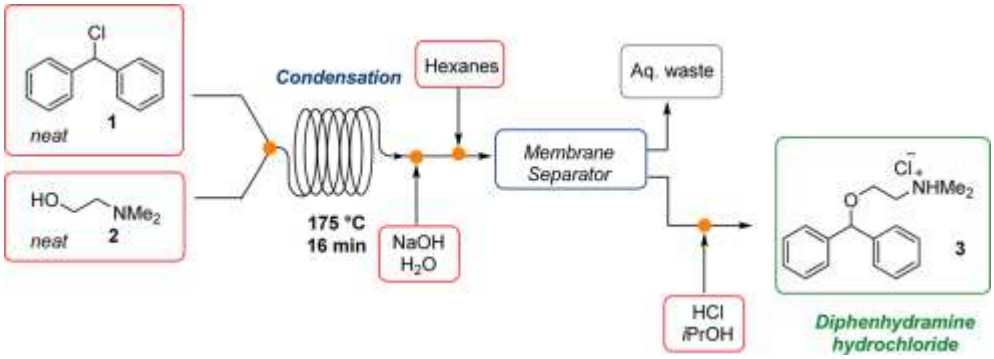
Flow chemistry has transformed organic synthesis through the rapid reaction optimization and efficient production of complex molecules (Webster et al., 2018). Its application in the synthesis of natural products and pharmaceutical intermediates is versatile and highly efficient (Gutmann et al. 2012). In the pharmaceutical industry, flow chemistry has accelerated the synthesis of drugs and intermediates, leading to rapid drug discovery and development cycles (Baumann et al., 2015). Flow systems enhance process safety and scalability (Cole et al., 2014). The synthesis of fine chemicals and petrochemicals has advantages, as precise reaction control is essential. These benefits include improved selectivity, reduced waste, and enhanced safety in the chemical

industry (Geyer et al., 2017; Sharma et al., 2016). Flow chemistry also plays a crucial role in polymer synthesis, enabling the production of polymers with customized properties and fine-tuned control over their molecular weight and composition (McLeod et al., 2014; Cantillo et al., 2016). Flow chemistry has been successfully applied in bioconjugation and bio-orthogonal applications. These applications support the efficient synthesis of biomolecular conjugates and novel bio-orthogonal reactions, thereby advancing research in drug delivery**,** diagnostics and chemical biology (Patterson et al., 2013; Adam et al., 2014).

Multistep synthesis of active pharmaceutical ingredients in flow

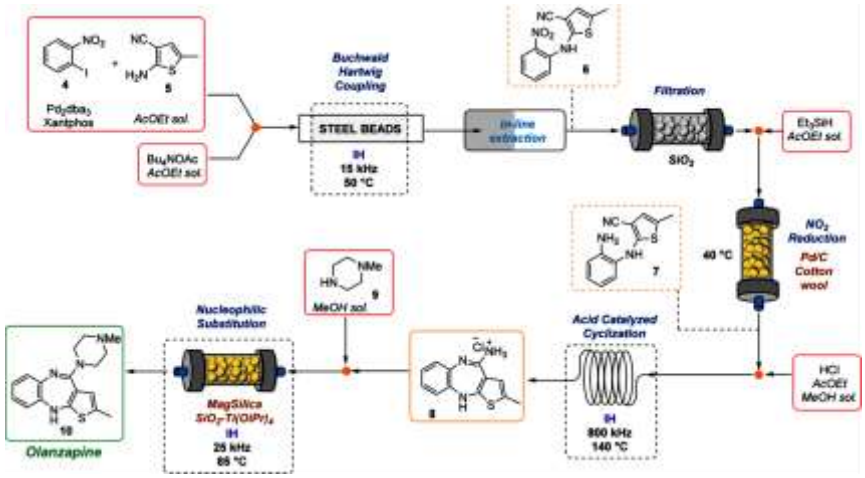
Scheme 1. Continuous Flow Synthesis of Diphenhydramine Hydrochloride: Antihistamine Medicine

In 2013, Jamison et al. developed a continuous flow process for the synthesis of diphenhydramine hydrochloride 3 from chlorodiphenyl methane 1 and dimethylethanolamine 2, minimizing waste and reducing purification steps and production time compared to existing batch synthetic routes.1



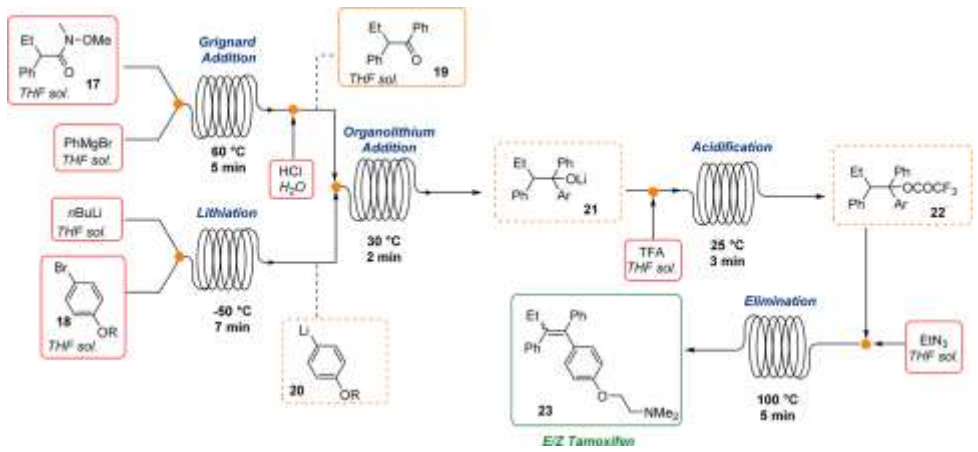
Scheme 2. Continuous Flow Synthesis of Olanzapine:

An Antipsychotic Drug In 2013, Kirschning et al. developed a multistep continuous-flow synthesis of olanzapine 10 using inductive heating (IH), which dramatically reduced the reaction time and increased the process efficiency.2



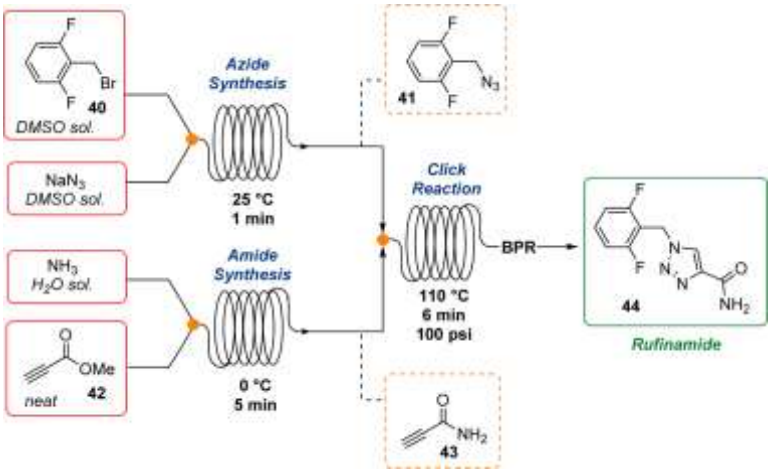
Scheme 3. Continuous Flow Synthesis of Tamoxifen: Anti-Cancer Drug

In 2013, Ley's research group developed a multistep synthesis of tamoxifen **23**, which is used in the treatment of all stages of breast cancer.4 This procedure combined four different chemical transformations into one stream and minimized manual intervention, thereby reducing the risk of handling organometallic reagents.



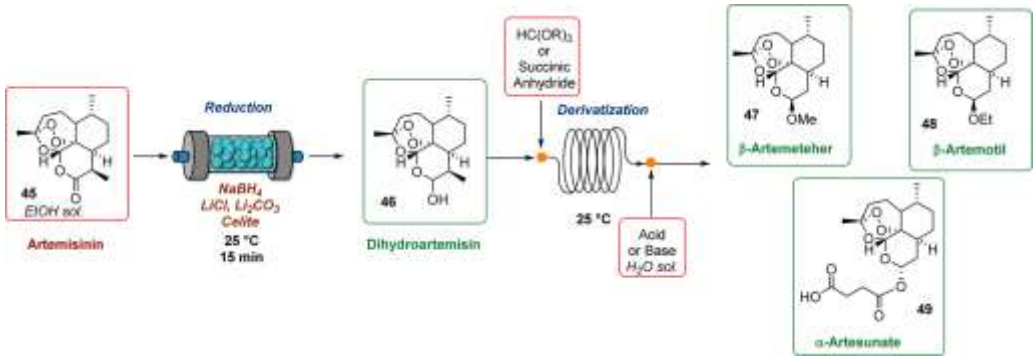
Scheme 4. Continuous Flow Synthesis of Rufinamide: An Antiepileptic Drug

In 2014, Jamison developed a continuous-flow synthesis of organic azides and their application in the multistep synthesis of the antiepileptic API rufinamide 44.7.



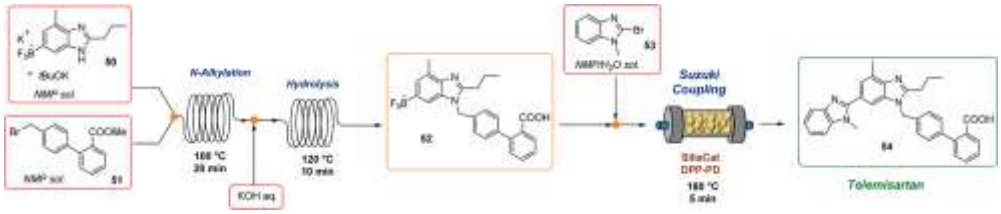
Scheme 5. Continuous Flow Synthesis of Four Antimalaria APIs

Malaria is a major health problem worldwide that affects hundreds of thousands of people annually. The most effective drug against malaria is artemisinin, an organic molecule extracted from *Artemisia annua plant.* In 2012, Seeberger et al. developed a multistep continuous-flow synthesis of artemisinin 45starting from dihydroartemisinic acid through a photooxidation process 8



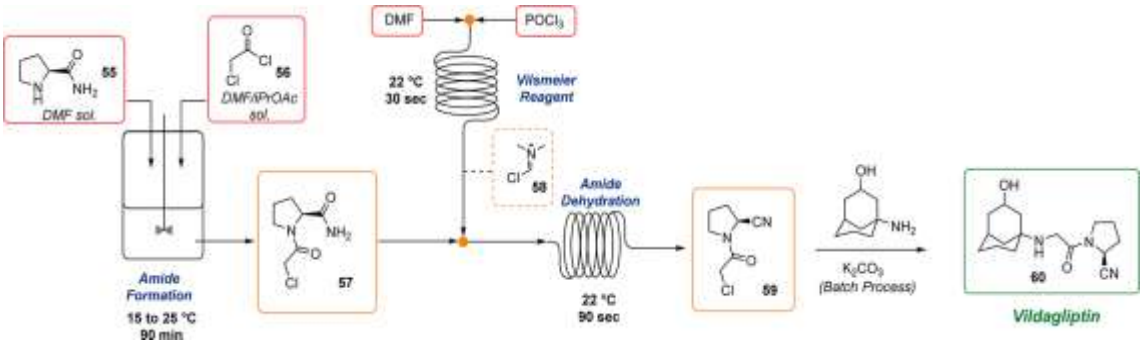
Scheme 6. Continuous Flow Synthesis of Telemisartan: Anti-hypertensive drug

Gupton et al. developed a continuous-flow convergent multistep synthesis of telemisartan10 that did not require intermediate purification or the use of solvents. This fully automated process represents a significant improvement over the traditional batch procedure.11



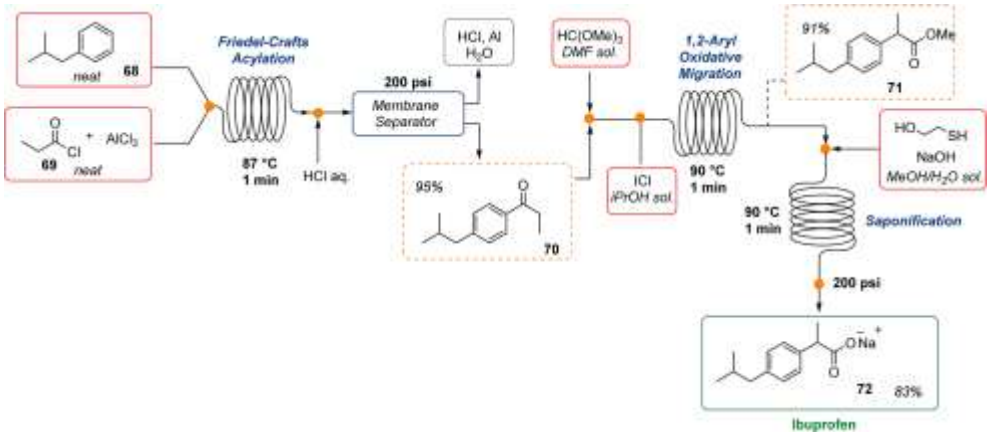
Scheme 7. Continuous Flow Synthesis of Vildagliptin: An antihyperglycemic

Sedelmeier reported the continuous flow synthesis of vildagliptin to increase the safety of the processes associated with the use of the Vilsmeier reagent (VR). .12



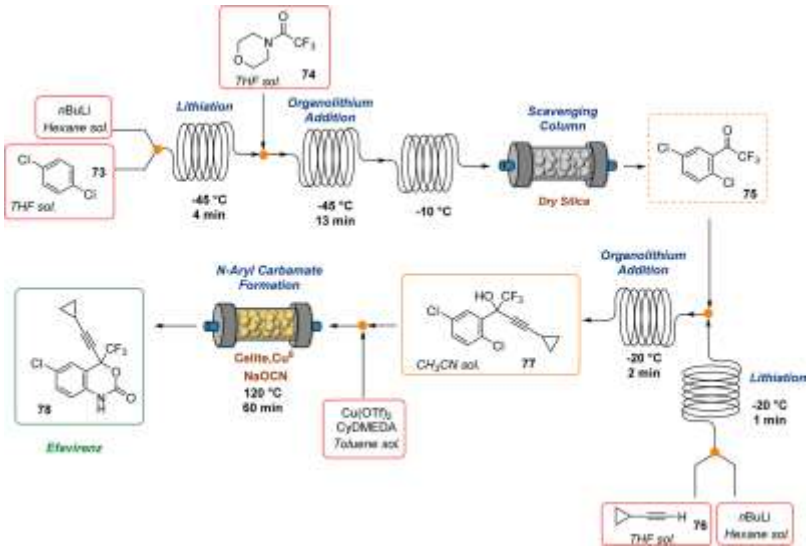
Scheme 8. Continuous Flow Synthesis of Ibuprofen: Nonsteroidal anti-inflammatory (NSAID)

Jamison et co-workers demonstrated 13 the continuous flow synthesis of ibuprofen, a generic pharmaceutical, ibuprofen 72. After 3 min, API 72 was prepared from inexpensive reagents with an overall yield of 83%.



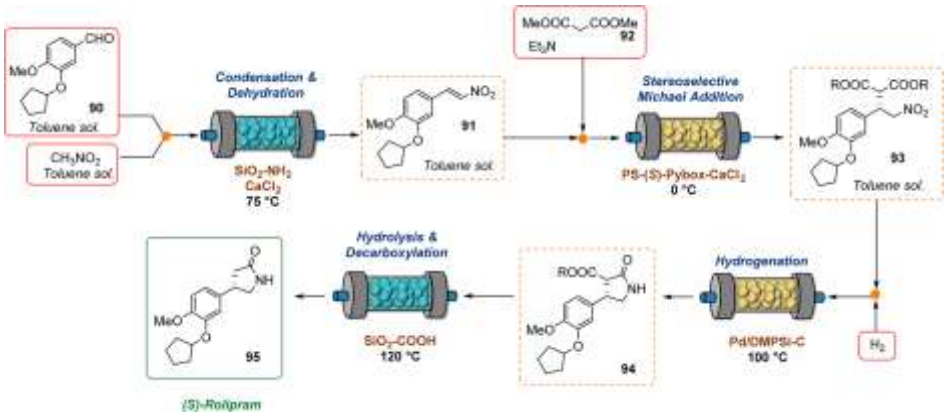
Scheme 9. Continuous Flow Synthesis of Efavirenz: Anti-HIV

Efavirenz, an essential drug for the treatment of HIV, is currently manufactured by Merck15 and Lonza16 through batch procedures involving four and five synthetic steps, respectively. In a recent study,17 Seeberger et al. developed a concise flow protocol for the preparation of efavirenz 78, leading to a shorter (three-step), cleaner, and safer synthetic pathway that avoided the use of toxic reagents and employed a new methodology for the introduction of the carbamate core ring.



Scheme 10. Continuous Flow Synthesis of (S)-Rolipram: An antidepressantdrug

Kobayashi et al. recently reported, for the first time, the constant-flow multistep synthesis of (S)-rolipram 95 using reactors containing solid-supported catalysts and reagents, without requiring any intermediate operation (Scheme 15).19



Conclusion

Flow chemistry represents a significant advancement in modern chemical synthesis, providing precise control over the reaction conditions and enabling the efficient production of complex compounds. Compared with conventional batch processing, continuous flow systems offer improved reaction safety, scalability, and reproducibility, making them particularly valuable in industrial and pharmaceutical applications. Despite these advantages, several challenges remain, including the development of fully integrated multistep systems, optimization of large-scale processes, and incorporation of advanced automation and monitoring technologies into the process. Addressing these limitations through continued research and technological innovation is essential for realizing the full potential of this technology. With sustained progress in reactor engineering and process design, flow chemistry is expected to play a pivotal role in shaping the future of sustainable and efficient chemical manufacturing processes.

Acknowledgment

The authors would like to express their sincere gratitude to Sandip University, Nashik, Maharashtra, for providing the necessary infrastructure, facilities, and academic support to carry out this work. We are thankful to our colleagues and faculty members for their valuable discussions, suggestions, and encouragement during the preparation of this review. The authors also acknowledge the contributions of researchers worldwide whose published work has significantly advanced the field of flow chemistry and formed the foundation of this study.

Financial support and sponsorship

Nil.

Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

References

1. Snead, D. R.; Jamison, T. F. Chem. Sci. 2013, 4, 2822.
2. Hartwig, J.; Ceylan, S.; Kupracz, L.; Coutable, L.; Kirschning, A. Angew. Chem., Int. 2013, 52, 9813
3. Kupracz, L.; Kirschning, A. Adv. Synth. Catal. 2013, 355, 3375.
4. Murray, P. R. D.; Browne, D. L.; Pastre, J. C.; Butters, C.; Guthrie, D.; Ley, S. V. Org. Process Res. Dev. 2013, 17, 1192.
5. Guetzoyan, L.; Nikbin, N.; Baxendale, I. R.; Ley, S. V. Chem. Sci. 2013, 4, 764.
6. Battilocchio, C., Deadman, B. J., Nikbin, N., Kitching, M. O., Baxendale, I. C., Ley, S. V. Chem. - Eur. J. 2013, 19, 7917.
7. Zhang, P.; Russell, M. G.; Jamison, T. F. Org. Process Res. Dev. 2014, 18, 1567.
8. Lévesque, F.; Seeberger, P. H. Angew. Chem., Int. Ed. 2012, 51,1706.
9. G. Gilmore, D. Kopetzki, J. W. Lee, Z. Horvath, D. T. McQuade, A. Seidel-Morgenstern and P. H. Seeberger, Chem. Commun. 2014, 50, 12652.
10. Martin, A.; Siamaki, A.; Belecki, K.; Gupton, B. J. Flow Chem. 2015, 5, 145.
11. (a) Ries, U. J.; Mihm, G.; Narr, B.; Hasselbach, K. M.; Wittneben, H.; Entzeroth, M.; Van Meel, J. C. A.; Wienen, W.; Hauel, N. H. J. Med. Chem. 1993, 36, 4040. (b) K. S. Reddy, N. Srinivasan, C. R. Reddy, N. Kolla, Y. Anjaneyulu, S. Venkatraman, A. Bhattach, T. Mathad, Org. Process Res. Dev. 2007, 11, 81. (c) L. J. Goossen and T. J. Knauber, Org. Chem. 2008, 73, 8631. (d) Kumar, A. S.; Ghosh, S.; Mehta, G. N. Beilstein J. Org. Chem. 2010, 6, 25.
12. Pellegatti L., Sedelmeier J. Org. Process Res. Dev. 2015, 19, 551
13. Snead, D. R.; Jamison, T. F. Angew. Chem Chem., Int. Ed. 2015, 54, 983.
14. Bogdan, A. R., Poe, S. L., Kubis, D. C., Broadwater, S. J., McQuade, D. T., Angew. Chem., Int. Ed. 2009, 48, 8547.
15. Pierce, M. E.; et al. J. Org. Chem. 1998, 63, 8536. (b) L. A. Radesca, Y. S. Lo, J. R. Moore, M. E. Pierce, Synth. Commun. 1997, 27, 4373.
16. Dai, D.; Long, X.; Luo, B.; Kulesza, A.; Reichwagen, J.; Guo, Y. (Lonza Ltd.) Process for the preparation of efavirenz by cyclization. PCT Int. Appl. WO2012097510, 2012.
17. Correia, C. A.; Gilmore, K.; McQuade, D. T.; Seeberger, P. H. Chem., Int. Ed. 2015, 54, 4945.
18. Ghislieri, D.; Gilmore, K.; Seeberger, P. H. Chem., Int. Ed. 2015, 54, 678.
19. Tsubogo, T.; Oyamada, H.; Kobayashi, S. Nature 2015, 520, 329.
20. Adamo, A., & Jensen, K. F. (2016). Microreactors for organic synthesis and catalysis. Angewandte Chemie International Edition, 55(20), 1-32.
21. Adamo A, Beingessner R. L., Behnam, M., Chen, J., Jamison, T. F., Jensen, K. F., Zhang, P. (2016). On-demand continuous-flow pharmaceutical production in a compact reconfigurable system. Science, 352(6281), 61-67.
22. Baumann, M., Moody, T. S., Smyth, M. G. (2016). Continuous-flow chemistry: Where are we now? Organic Process Research and Development, 20(1), 2-25.
23. Baumann, M., Moody, T. S., and Smyth, M. G. (2016). Continuous-flow chemistry: Where are we now? Organic Process Research and Development, 20(1), 2-25.
24. Baxendale, I. R., Deeley, J., Griffiths-Jones, C. M., Ley, S. V., Saaby, S., & Tranmer, G. K. (2015). Integration of continuous flow processing into the synthesis of pharmaceutical agents. Organic Process Research & Development, 19(10), 1421-1451.