Stereoselective Synthesis of Multifunctional and Bioactive Molecules via Asymmetric Organocatalysis

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Asymmetric catalysis is superior to classical resolution and chiron/auxiliary approaches and is currently reaching the level of mimicking biological processes. Asymmetric organocatalysis, viz. performing organic reactions under the catalytic influence of small chiral organic molecules, in particular, has developed in the last twenty five years as a powerful alternative to metal and enzyme mediated reactions. These reactions do not require anhydrous and anaerobic medium and often proceed under mild and environmentally friendly conditions in the presence of substoichiometric amounts of chiral organocatalysts. Various multi-component and cascade reactions are now efficiently catalyzed by small, simple, chiral organic molecules. Selected applications of asymmetric organocatalysis in the synthesis of complex molecules reported from our laboratory will be discussed in this lecture as outlined below. Since aminophosphonate moiety mimics the tetrahedral transition state of carboxylate in peptide bond hydrolysis, catalytic asymmetric approaches to synthesis of aminophosphonates is of considerable interest. Corresponding aminosulfones and amino acids, especially those bearing a tetrasubstituted α-chiral center, are also sought-after targets because of their synthetic and biological applications. Therefore, α-aminophosphonates and their aminosulfone and aminocarboxylate analogs have been synthesized in our laboratory via facile Michael addition of various phosphonates, sulfones and esters to electron deficient alkenes in the presence of chiral thiourea and squaramide organocatalysts. Asymmetric organocatalyzed cascade reactions of various 1,3-dicarbonyl compounds, including curcumins, with nitroalkenes and alkylideneoxindoles provide access to complex multifunctional scaffolds. Finally, enantioselective aldol reactions in water in the presence of a heterogenized organocatalyst and approaches to development of novel polycyclic cage-based catalysts via optical resolution will be described.

Selected Recent References

[8] G. L. Tejashree, A. Bhattacharjee and I. N. N. Namboothiri, *Org. Lett.* **2026**, *28*, 3342.
[7] G. L. Tejashree, A. Dave, N. Kumbhakarna, A. Chowdhury and I. N. N. Namboothiri**,** *Chem. Commun.* **2024,** *60*, 14142 (Feature Article).
[6] C. Demeese, C. Lods, D. A. Buisson, E. Gravel, I. N. N. Namboothiri and E. Doris, *Chem. Eng. J.* **2023**, *476*, 146702.
[5] C. S. Sankara, S. Bhagat, A. Chandra and I. N. N. Namboothiri, *Eur. J. Org. Chem.* **2023**, e202300069.
[4] B. Laha, A. Suresh and I. N. N. Namboothiri, *Org. Biomol. Chem.* **2023**, *21*, 1872.
[3] G. L. Thejashree, E. Doris, E. Gravel and I. N. N. Namboothiri, *Eur. J. Org Chem.* **2022**, e202201035 (review).
[2] K. Bera, N. Ayyagari, N. S. Satam and I. N. N. Namboothiri, *Org. Biomol. Chem.* **2020**, *18*, 140.
[1] I. N. N. Namboothiri, M. Bhati, M. Ganesh, B. Hosamani, T. V. Baiju, S. Manchery and K. Bera, Catalytic Asymmetric Reactions of Conjugated Nitroalkenes, CRC Press, Taylor & Francis Group, Boca Raton, USA, **2020** (Book).