Enantioselective aza-Henry Reaction of Arylnitromethane using Homogeneous Bronsted Acid-Base Catalyst under Intermittent-Flow Conditions with a Recycle

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Growing knowledge in the area of continuous processing has established that flow methods could serve as an effective substitute to the majority of batch techniques providing unique advantages and straightforward solutions to the challenging chemical reactions. We have transformed a standard enantioselective batch aza-Henry reaction into intermittent-flow process. This novel platform produces valuable synthetic building blocks on a multigram scale with an increased overall intensity while addressing the common safety concerns associated with utilization of nitroalkanes. Organocatalyst was separated and continuously recycled providing reduced catalyst loadings. This project showcases successful synergy between efficiency of organocatalysis and transformative power of continuous processing. It also allows to effectively integrate green chemistry (reduced production footprint), atom economy (minimized reactor size, solvent volumes and application of catalyst recycle) and higher safety margins (decreased safety risks, defined operating space for nitroalkanes); overall these advantages lead to a significant cost benefit. The designed process could be utilized for a large scale synthesis of differentially protected diamines which are useful building blocks with a broad scope of applications.