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Metal-Free Approaches towards N-Heterocycles and Diarylmethanes under Batch as well as Continuous-Flow Conditions

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Abstract:

Nitrogen-based heterocycles are considered as the most important class of organic compounds as they are involved in many biological processes. Moreover, many N-heterocyclic cores such as indole, dihydroquinoline, acridine, etc. are often found as integral part of many natural and unnatural significant molecules and possess various therapeutic properties such as anti-cancer, anti-bacterial, anti-viral, anti-HIV, etc. Due to their biological importance and structural diversity, they are an attractive target for many synthetic and medicinal chemists. Therefore, developing practical and metal trace-free protocols for their synthesis is highly desirable. In the present work, we have utilized p-QMs and ortho-aminobenzyl alcohols to synthesize N-containing heterocycles and diarylmethanes under batch and continuous-flow conditions. Part A of this work includes the synthesis of 2,3 di-substituted indoles, dihyroquinolines, and tetrahydroacridine derivatives from the reaction of 2-(tosylamino)aryl-substituted p-QMs and ortho-aminobenzyl alcohols with suitable coupling partner under metal-free conditions, the second part of this work describes the 1,6-conjugate addition of nitroalkanes on p-QMs to access diarylmethanes in continuous flow reactor (microreaction technology) under organocatalytic conditions. We have also demonstrated the advantage of a continuous flow reactor over the batch process for this particular transformation.

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