

Flow Parallel Synthesizer for Multiplex Synthesis of Aryl Diazonium Libraries via Efficient Parameter Screening

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The emergence and development of miniaturized parallel flow platform enables efficient and selective synthesis of drug and lead molecules by exploring synthetic methodologies and screening for optimal conditions, which would be of transformative advance. Herein, we report a metal-based flow parallel synthesizer that enables multiplex synthesis of libraries of compounds and efficient screening of parameters. This miniaturized synthesizer, equipped with a unique built-in flow distributor and n number of microreactors, can execute multiple types of reactions in parallel under diverse conditions, including photochemistry. Diazonium-based reactions are explored as a test case by distributing the reagent to 16 ($n=16$) capillaries to which various building blocks are supplied for the chemistry library synthesis at the optimal conditions obtained by multiplex screening of 96 different reaction variables in reaction time, concentration, and product type. The proficiency of the flow parallel synthesizer is showcased by multiplex formation of various C-C, C-N, C-X, and C-S bonds, leading to optimization of 24 different aryl diazonium chemistries.