From Batch to Flow: Chemo-Enzymatic Asymmetric Synthesis of Piperidine Scaffolds

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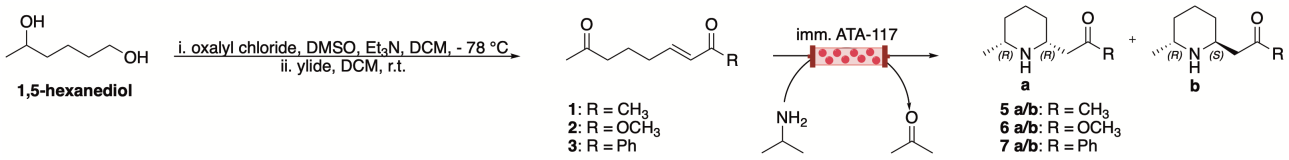
A pyridoxal 5'-phosphate-dependent transaminase (ATA-117) was selected and covalently immobilized on Eupergit®C to enhance its operational stability and reusability. A stereoselective transamination, followed by a spontaneous intramolecular aza-Michael reaction (**Scheme 1**), was performed to synthesize natural (-)-pinidinone (**5a,** 10.1021/jacs.6b07024). The reaction was then optimized in a continuous flow system evaluating substrate concentration, isopropylamine equivalents, reaction temperature, residence time, type and amount of cosolvent.



Scheme 1: Chemo-enzymatic asymmetric flow synthesis of 2,6-disubstituted piperidines.