Parallel Kinetic Resolution of N-Heterocycles by N-Acylations in Flow

Significance: A flow system for parallel kinetic resolution of N-heterocycles by using polymer-supported pseudoenantiomeric acylating agents was developed. A racemic mixture of heterocycles 1 was converted into the corresponding enanti-enriched amides 4 and 5 in 17–50% yield by using a flow-reaction system with acylating agents 2 and 3 (0.5 mol equiv each).

Comment: The resulting amides 4 and 5 were readily deprotected to give the corresponding free amines. Thus, for example, (R,S)- and (S,R)-mefloquine (1e) were obtained from a 1:1 mixture of amides 4e and 5e by selective deprotection without detectable epimerization (60–90% yield).