In a significant recent advance, Hoffmann reported the availability of enantioenriched α-chloroalkyl Grignard reagents (2, M = MgCl) via sulfoxide ligand exchange (SLE) from homochiral α-chlorosulfoxides (1).\(^1\) Inspired by the work of Matteson,\(^2\) we reasoned that deployment of Hoffmann-type carbenoids in the chain-extension of boronic esters would likely result in a stereospecific reagent controlled homologation (StReCH) process (i.e., 3 to 4). Iterative application of this new type of transformation could lead to a unified asymmetric synthetic technique in which constitution and stereochemical features are directly programmed by the carbenoid presentation sequence (e.g., 4 to 5). It was previously established that Mg- and Li-carbenoids (Li better) generated via SLE, chain-extend boronates in the desired manner in up to 98% ee.\(^3\) StReCH becomes particularly powerful upon its iterative application and we are currently investigating the viability of an automated implementation of the process using novel microreactor technology. Preliminary results concerning this new project will be presented.

References:

