A New Paradigm for Stereocontrol in Organocatalysis

Detailed mechanistic studies of several reactions catalyzed by diphenylprolinol ether catalysts led to the proposal that enantioselectivity is determined not in the stereogenic bond-forming step but is controlled by the relative stability and activity of diastereomeric intermediates downstream from this step in the catalytic cycle. Equilibration of intermediates prior to a definitive irreversible step combines kinetic and thermodynamic influences on ultimate product selectivity in a classic Curtin-Hammett scenario. Evidence is offered to suggest that this concept may represent a general phenomenon for pyrrolidine-based catalysts lacking an acidic directing proton. Implications for catalyst and reaction design are discussed.