

Ligand Tuning as a Tool for the Discovery of New Catalytic Asymmetric Processes

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Abstract: In this era of heightened environmental awareness and ever-increasing demand for higher efficiency from chemical processes, one of the major challenges facing organic synthesis is the utilization of abundantly available carbon sources as precursors for more advanced intermediates. The dual problems of activation of thermodynamically stable precursors and their stereoselective incorporation pose new challenges, solutions of which may have broader implications in asymmetric catalysis. This review summarizes our recent efforts to discover broadly applicable control elements in key enantioselective carbon-carbon and carbon-hydrogen bond-forming reactions. Transition metal complexes of 1,2-diol phosphinites derived from readily available monosaccharides catalyze a variety of asymmetric reactions of prochiral olefins including Markovnikov addition of HCN to vinyl arenes and hydrogenation of dehydroamino acids. Enantioselectivities of these reactions can be optimized through steric and electronic tuning of the bis-phosphinite ligand system. Both *R* and *S* enantiomers of the precursors of prototypical 2-arylpropionic acids and of various α -amino acids can be prepared by these routes. We have also discovered new protocols for a nearly quantitative and highly selective codimerization of ethylene or propylene, and various functionalized vinylarenes and strained olefins. Various strategies for stereochemical control in an enantioselective version of this reaction will be discussed. These include design and synthesis of new ligands and applications of the 'hemi-labile ligand concept'. During these investigations important synergistic relationships between such ligands and coordinating properties of various counter ions were also uncovered. These discoveries may contribute to the discovery of more selective homogeneous catalysts.

Dedicated to Professor Henri B. Kagan in recognition of his seminal contributions to catalytic asymmetric synthesis

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