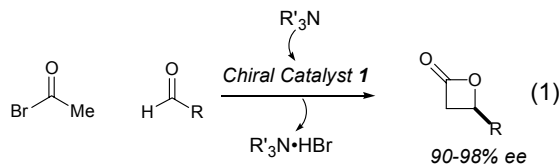


Reaction and Catalyst Designs for Asymmetric Automated Synthesis

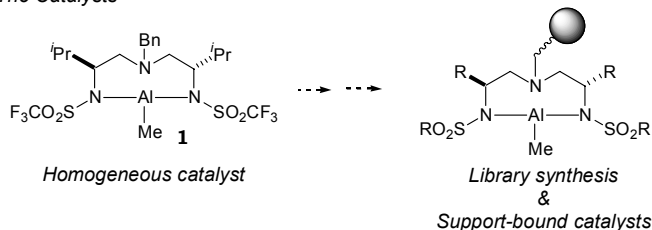
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The development of asymmetric catalytic reaction methodology having applications in automated synthesis will be presented. Our group has developed of acyl halide-aldehyde cyclocondensation (AAC) reactions as a strategy for executing catalyzed asymmetric aldol bond constructions (eq 1). In developing this reaction technology, library synthesis was used in identifying the catalyst complex **1** that offered optimum enantioselection in the ketene-aldehyde [2+2] cycloadditions. Methods for preparing ligand and catalyst structures on solid support as well as the use of polymer-bound catalyst complexes will be described.



The Catalysts



The optically active β -lactones emerging from the asymmetric AAC reactions constitute exceptionally versatile platforms for asymmetric synthesis due to their unique bifunctional electrophilic character. The utility of these optically active β -lactones as surrogates for asymmetric acetate and propionate aldol reactions as well as precursors to enantiomerically enriched allene acetic acid derivatives will be presented; these reaction technologies form the cornerstone for efforts directed toward preparing the naturally occurring anticancer agents laulimalide and rhazinilam. Furthermore, the optically active β -lactones provide especially efficient precursors to β -azido acids, direct progenitors of β -amino acids. Since peptide-like structures derived from β -amino acids, “ β -peptides,” have emerged as increasingly promising chemotherapeutic agents, we have begun a program directed toward the general synthesis of β -peptide structures. Efforts directed toward developing enantiomerically enriched β -azido acids as building blocks for solid phase and automated β -peptide synthesis will also be described.

