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Doctoral dissertation: “Synthesis and transformations of chiral β -amino alcohols with pyridine and 1-phenylethylamine fragments.”

Abstract

The project was aimed at the design and development of novel modular chiral ligands-catalysts for asymmetric reactions. The key concept was an introduction of additional metal complexing moieties of pyridine and 2,2'-bipyridine to the chiral scaffold offered by α -phenylethylamine (α -PEA). We synthesized new pyridine-substituted epoxides that were subsequently opened with α -PEA in the $\text{Sc}(\text{TfO})_3$ – catalyzed reaction. The prepared diastereomeric β -amino alcohols were successfully separated. In the next step, these products were transformed into the respective chiral diamines via azides. In the case of an α -pyridine amino alcohol, the first formed product was the aziridine derivative, then stereoselectively opened to the azido-amine. The Staudinger reduction of azides gave the desired products. The chiral diamines reacting with the appropriate salicylaldehydes were converted into the corresponding mono-aldimines. We also synthesized sulfur- and selenium-containing chiral ligands with phenylsulfanyl (-SPh) and phenylselenyl (-SePh) groups. The other experiments have shown that the corresponding cyclic sulfin- and sulfonamides could be obtained from chiral β -amino alcohols by simple reaction with thionyl chloride. These cyclic synthetic intermediates underwent the stereospecific $\text{S}_{\text{N}}2$ reactions, and the desired substitution products were formed. The obtained modular catalysts were tested in several asymmetric reactions: aldol, Henry, Michael reactions, sulfoxidation, and Tsuji-Trost reactions. The last one, the Pd-catalyzed process, led to up to 75% ee. The observed sense of asymmetric induction resulted from the nucleophilic attack at the position trans vs. the coordinated pyridine nitrogen.