LIGAND DESIGN IN THE ASYMMETRIC SYNTHESIS OF TERTIARY ALCOHOLS

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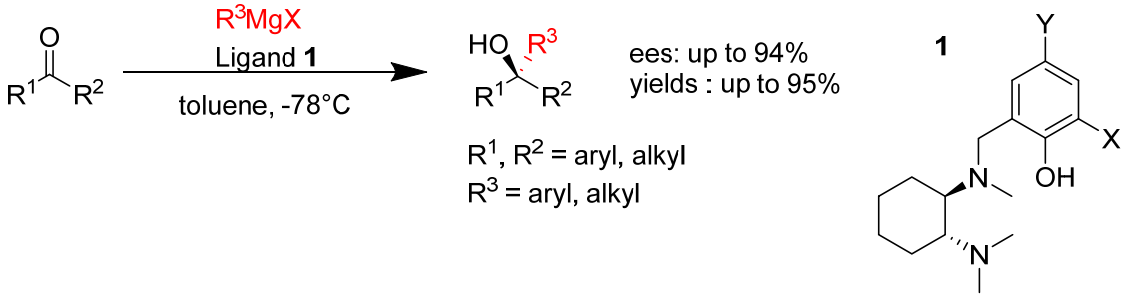
Chiral tertiary alcohols constitute an important class of biologically active molecules.[1] However their synthesis remains problematic. An enantioselective 1,2-addition of Grignard reagents to ketones remains highly desired. Few methodologies exist for stereoselective synthesis of tertiary alcohols by direct 1,2-addition of Grignard reagents to ketones, and to best of our knowledge, only two cases have been reported to date where high enantioselectivity was obtained in the absence of metals other than magnesium.[2]



We followed on from previously successful research in the group in which a semi-rational ligand design was used to synthesize a class of tridendtate ligands -**1.**Their use in the asymmetric 1,2-addition of Grignard reagents to ketones allows generation of chiral tertiary alcohols in high yields and enantioselectivities.[3] We now describe a late stage diversification strategy for the synthesis of highly stereoselective biaryl ligands for use in this transformation. Furthermore, we detail our attempts towards a multivariate statistical model.[4] In this we parameterize the reaction in terms of ligand substitution; to both predict effective ligands and to elucidate mechanistic details.

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