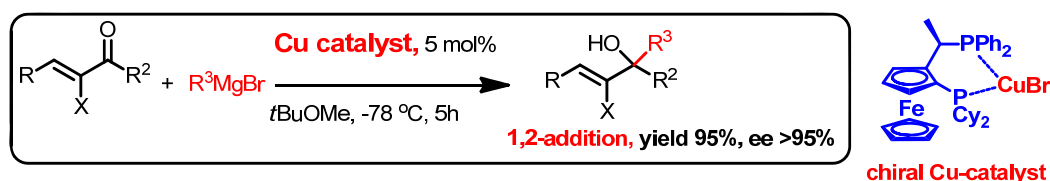


Synthesis of new chiral ferrocenyl diphosphine ligands for application in catalytic asymmetric 1,2-addition of organometallics to ketones

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Chiral tertiary alcohols are important structural motifs which are present in a variety of natural products and pharmaceutical compounds.¹ Recently, we described the first copper catalyzed asymmetric 1,2-addition of Grignard reagents to enones and aromatic ketones.^{2,3} Breaking with the conventional wisdom that Cu(I)-based reagents give selective 1,4-addition, we showed that with catalytic amount of a copper (I) salt in combination with a chiral ferrocenyl diphosphine ligand we can access chiral tertiary alcohols in high yield and enantioselectivity.



Despite great advancement using this new methodology there are still several challenges associated with this chemistry. In particular linear Grignard reagents provide low values of enantioselectivity compared to branched ones. Furthermore, good regioselectivity is only obtained for alpha substituted enones. For non-substituted enones, a mixture of both 1,2- and 1,4-addition products are obtained with low enantioselectivity.

Here we would like to report on the synthesis of new chiral ferrocenyl diphosphine ligands for application in the catalytic asymmetric 1,2-addition of organometallics to carbonyl compounds. By changing the electronic and steric properties of the ligand we want to address these major challenges. Number of ligands have been synthesized and screened for this purpose. Preliminary results indicate that by tuning the electronic properties of the phosphine moiety in the ligand structure we can affect the regioselectivity between 1,2- and 1,4-addition products.

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