UNIVERSITAT ROVIRA I VIRGILI
SCREENING OF MODULAR CARBOHYDRATE LIGAND LIBRARIES
IN ASYMMETRIC METAL-CATALYZED C-C AND C-X BOND FORMATION REACTIONS
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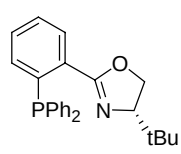
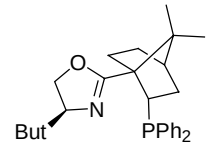
4. Pd-catalyzed asymmetric Heck reaction

4.1. Background

In the last few years, the phosphine-oxazoline ligands have emerged as suitable ligands for the intermolecular Heck reaction. Two of the most representative examples of this type of ligands are the PHOX ligands developed by Pfaltz and coworkers[1] and the phosphine-oxazoline based on ketopinic acid developed by Gilberston and coworkers[2] (Figure 1). Despite these successes, ligands that provide good regio- and enantioselectivities usually have two considerable drawbacks: (1) reaction times are usually long and (2) they are prepared from expensive chiral synthons or in tedious synthetic steps. Therefore, it is very important to develop ligands that induce higher rates and selectivities (regio- and enantioselectivities) based on simple starting materials in this reaction. More research is therefore needed to study the possibilities offered by other classes of ligands in this process. As we discussed in the introduction (Chapter 1), in the last few decades carbohydrate ligands have been widely used in asymmetric catalysis. However, their full potential in providing chiral ligands has hardly been studied in Heck reactions. Only two reports on the highly enantioselective palladium-catalysed asymmetric Heck reaction have been reported using these systems.[3] To our knowledge, phosphite-oxazoline, phosphite-phosphoroamidite and monophosphite ligands have not been applied before in this process.



Pfaltz's Ligand



Gilbertson's Ligand

Figure 1. Representative phosphine-oxazoline ligands for asymmetric Pd-catalyzed Heck reactions

In chapter 4.2, we report the application of the phosphite-oxazoline ligand library **L1**-**L4a-g** previously synthesised in chapter 3 in the asymmetric Pd-catalyzed Heck reaction. We found that the degree of isomerization and the effectiveness in transferring the chiral information in the product and the activity can be tuned by correctly choosing ligand components (phosphite and oxazoline substituents). Excellent activities (up to 100% conversion in 10 minutes), regio- (up to >99%) and enantioselectivities (ee's up to 99%) were obtained in a wide range of substrates and triflate sources. Unfortunately, the preliminary studies using the phosphite-phosphoroamidite **L6a-c** and monophosphite **L7**-**L11a-f** ligand libraries in several reaction conditions showed low activities and selectivities. Therefore, the former library resulted to be inactive while the later showed low activities (< 20% yield after 4 days) and low regio- and enantioselectivities (< 10%).

4.1.1. References

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