UNIVERSITAT ROVIRA I VIRGILI
SCREENING OF MODULAR CARBOHYDRATE LIGAND LIBRARIES
IN ASYMMETRIC METAL-CATALYZED C-C AND C-X BOND FORMATION REACTIONS
Yvette Angela Mata Campaña
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7. Conclusions

1. Chapter 3. *Pd-catalyzed asymmetric allylic substitution*. The conclusions of this chapter can be summarized as follows:

- In the asymmetric Pd-catalyzed allylic substitution reactions using chiral phosphite-oxazoline ligands we observed important effects of the oxazoline substituents and the axial chirality and the substituents of the biaryl moieties. However, the effects of these parameters depended on each substrate. High enantioselectivities (up to 99%) and good activities have been achieved in a wide range of substrates with different steric and electronic properties.

The study of the Pd-1,3-diphenyl, 1,3-dimethyl and 1,3-cyclohexenyl allyl intermediates by NMR spectroscopy made it possible to understand the catalytic behaviour observed. This study also indicated that the nucleophilic attack takes place predominantly at the allylic terminal carbon atom located *trans* to the phosphite moiety.

- Asymmetric substitution reactions with catalyst precursors containing the phosphite-phosphoroamidite ligands showed that enantiomeric excesses depend strongly on the substituents at the *para* positions of the biphenyl moieties. However, these effects were different depending on the substrate in study. Enantiomeric excesses of up to 89% with high activities were obtained for *rac*-1,3-diphenyl-3-acetoxyprop-1-ene, *rac*-(*E*)-ethyl-2,5-dimethyl-3-hex-4-enylcarbonate and *rac*-3-acetoxycycloheptene. For the monosubstituted linear substrate 1-(1-naphthyl)allyl acetate, these ligands proved to be inadequate in terms of regioselectivities. However, we obtained good enantioselectivity by carefully selecting the substituents on the *para* position of the biphenyl moieties (ee's up to 72%).

If we compare these results with those from the catalyst precursors containing the previous phosphite-oxazoline ligands, we found that the replacement

of the oxazoline moiety by a phosphoroamidite group decreased enantioselectivities and versatibility.

- Asymmetric allylic alkylation with catalyst precursors containing the sugar-based monophosphite ligand library showed that the catalytic performance is highly affected by the size of the sugar backbone, the configurations at C-3 and C-4 of the ligand backbone and the type of substituents/configurations in the biaryl phosphite moiety. Unfortunately, low-to-moderate enantioselectivities (up to 46%) were obtained.

2. Chapter 4. *Pd-catalyzed asymmetric Heck reactions*. The conclusions of this chapter can be summarized as follows:

- In the asymmetric Pd-catalyzed Heck reactions with catalysts precursors based on phosphite-oxazoline ligands, 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 (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.

3. Chapter 5. *Ni-catalyzed asymmetric addition of trialkylaluminium to aldehydes*. The conclusions of this chapter can be summarized as follows:

- In the asymmetric Ni-catalyzed 1,2-addition of trialkylaluminium to aldehydes with catalysts precursors based on phosphite-oxazoline and phosphite-phosphoroamidite ligands, we found that the selectivity depends strongly on the type of functional group attached to the carbohydrate backbone, on the steric properties of the oxazoline substituents and on the substrate structure. Enantioselectivities up to 59% were obtained using the catalyst precursor containing the phosphite-oxazoline ligand **L3a**.

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- In contrast to what we observed with the previous two ligand libraries, using sugar-based monophosphite ligands in the asymmetric Ni-catalyzed 1,2-addition of trialkylaluminium to aldehydes provides high enantioselectivities (up to 94% ee) and activities in different substrate types, with low catalysts loadings and without excess of ligand.

4. Chapter 6. *Cu-catalyzed asymmetric 1,4-conjugated addition of trialkylaluminium reagents to enones*. The conclusions of this chapter can be summarized as follows:

- Using phosphite-oxazoline and phosphite-phosphoroamidite ligands as chiral auxiliaries in the asymmetric Cu-catalyzed 1,4-conjugated addition of trialkylaluminium reagents to several enones provides good enantioselectivities (up to 80% ee).

- In the asymmetric Cu-catalyzed asymmetric 1,4-conjugated addition of trialkylaluminium reagents to several enones with catalysts precursors based on sugar monophosphite ligands, we found good activites and enantioselectivities up to 57% ee.