

5. Ni-catalyzed asymmetric addition of trialkylaluminium to aldehydes

5.1. Background

The catalytic addition of organoaluminium reagents to aldehydes as a route to chiral alcohols has attracted much attention, since many chiral alcohols are highly valuable intermediates for preparing chiral pharmaceutical and agricultural products. Despite the organoaluminium reagents are economically obtained in industrial scale, their use is rare. In this respect, the few successful catalysts developed for the enantioselective addition of trialkylaluminium to aldehydes can be grouped in two types. The first group are the titanium complexes that usually afford high enantioselectivities, but the high catalyst loadings (10-20 mol %) and the slow turnover rate hamper their potential utility. The second ones are the recently studied nickel complexes that provide enantioselectivities similar to those using titanium complexes but with low catalyst loadings (1 mol %). For the latter group, only Woodward and coworkers reported the successful use of phosphoroamidite ligands as chiral source. Despite this success, the results indicate that an excess of ligand ($L/Ni = 2$) is necessary for high ee's to be achieved. More research is therefore needed to study the possibility offered by other ligands for this transformation.

In this chapter, we report the application of the three carbohydrate-based ligand libraries described in Chapter 3 (phosphite-oxazoline (**L1-L5a-i**), phosphite-phosphoroamidite (**L6a-c**) and monophosphite (**L7-L11a-f**) in the asymmetric Ni-catalyzed 1,2-addition of trialkylaluminium reagents to aldehydes. More specifically, in section 5.2 we report the application of the glucopyranoside phosphite-oxazoline (**L1-L5a-i**) and phosphite-phosphoroamidite (**L6a-c**) ligand libraries. Our results indicated that selectivity depended 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. The best enantioselectivities (ee's up to 59%) were obtained using the catalysts precursor containing the phosphite-oxazoline ligand **L3a** in the 1,2-addition of several *para*-substituted aryl aldehydes. In section 5.3, we report the application of the modular sugar-based monophosphite ligand library **L7-L11a-f** for the Ni-catalyzed 1,2-addition of trialkylaluminium reagents to aldehydes. In contrast to what we observed in section 5.2 with this monophosphite ligand library, we obtained high activities and enantioselectivities (ee's up to 94 %) in different substrate types with low catalyst loading (1 mol %) and without excess of ligand. Systematic variation of the sugar backbone, the substituents at the phosphite moieties and the flexibility of the ligand backbone, the monophosphite ligand **L7c** was found to be optimal.