

## *Evaluation*

In this section of the thesis the results obtained in this PhD project are evaluated in view of the IOP objectives and justifications.

New, active and selective catalysts were developed for the asymmetric transfer hydrogenation of ketones, which was the main objective of this research project. Through this route chiral alcohols can be produced under mild conditions without the formation of any byproducts.

Two different active catalytic systems were developed based on ruthenium(II) and iridium(I) with chiral nitrogen donor ligands. The chiral ligands consist of a two-carbon backbone, in which the chirality is present, and two donating atoms.

In the ruthenium(II) catalysed reduction of ketones anionic N,O-chelating ligands proved to be very successful. Ligand optimisation resulted in the best amino alcohol ligand developed so far, giving rise to enantioselectivities of up to 97%.

For the iridium(I) system a new class of neutral N,S-chelating ligands was developed. To different types of hydrogen donors were used in the iridium(I)-amino sulf(ox)ide catalysed transfer hydrogenation of ketones. Enantioselectivities of up to 97% were obtained.

The two catalytic systems form among the most active catalytic systems found so far for the asymmetric hydrogen transfer reactions.

A better insight in the ligand structure-enantioselectivity relationship was created based on experiments and theory. The most important positions in the ligand structure were determined for obtaining high enantioselectivities.

An additional objective of this research project was the development of catalysts for the transfer hydrogenation of functionalised ketones. Generally, the presence of functional groups in ketones gives rise to a dramatic decrease in both the activity and selectivity of the catalyst.

The asymmetric reduction of various functionalised ketones resulted in high chemoselectivities to the reduction of the C=O bonds. The obtained enantioselectivities were moderate in most cases and high for the reduction of acetylenic ketones. Hence, new catalysts need to be developed to meet the demands of fine-chemical industries for the reduction of some of these functionalised ketones.

In view of this, new techniques in rapid screening of the catalytic reactions would be very useful. Such a high throughput screening technique was developed for the transfer hydrogenation of ketones based on IR spectroscopy. Using this technique, the performance of catalysts can efficiently be determined by monitoring the reverse reaction.

From an industrial point of view, transfer hydrogenation is one of the most attractive methods for the transformation of prochiral ketones to chiral alcohols. At this moment some pilot-scale plants are operative using this method, which would not have been possible without the catalyst developments during the last five years.<sup>1</sup> Part of the work described in this thesis is patented by DSM Research.

1. J.H. de Vries, personal communication.