

# InCatT catalyst library: the key to rapid catalyst finding

## A guide to InCatT libraries of catalysts

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**Rapid catalyst finding is key for the chemical industry in which time to market is essential, such as the pharmaceutical and fine chemical industry. As for many new chemical conversions the catalyst needs to be tailored to get the required activity and selectivity of a catalytic process, and thus catalyst screening protocols have been developed. The success of such screening protocol largely depends on the size and diversity of the catalyst libraries. For asymmetric transformations this translates to a large and diverse set of chiral ligands. In this application note, InCatT B.V. describes how their unique catalyst libraries work and can be employed in the screening of homogeneous catalysts.**

## Introduction

Combinatorial chemistry approaches and high throughput catalyst screenings have been demonstrated to be increasingly important in the field of asymmetric catalysis, and developments in both academia and industry underline the relevance. For such an approach catalyst libraries are required. For the generation of catalyst libraries for asymmetric transformation, i.e. for the generation of chiral compounds in enantiopure form, the use of a library of chiral ligands is required. Whereas monodentate ligands are generally easier to prepare, bidentate ligands generally provide a more well defined chiral environment around the active site. Supramolecular ligands form bidentate ligands by self-assembly of ligand building blocks that are generally easy to prepare, and as such combine the advantages of mono and bidentate ligands. For combinatorial approaches it is a particularly powerful strategy as the number of catalysts grows exponentially with the number of synthesized building blocks. For this reason, InCatT relies for a large extend on such technology, but also uses commercially available libraries of catalysts to maximize the success rate of our screenings protocols. Our catalysts libraries will be described in the following sections, highlighting the diversity and strength of each families of catalysts.

## Homogeneous catalysts

Homogeneous catalysis has a very important role in the chemical industry and stands out specifically in performing chiral transformations. The asymmetric hydrogenation of prochiral substrates is one of the most powerful methods for the synthesis of chiral compounds as this reaction is very general as most chiral centers have hydrogen atom, and the reaction is functional group tolerant. The selectivity of a reaction strongly depends on the catalyst used, and for new substrates the screening of numerous homogeneous catalysts is often necessary to

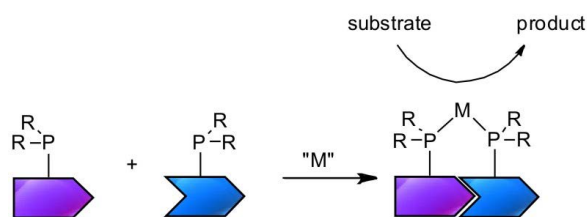


Fig. 1: Conceptual representation of InCatT's supramolecular bidentate catalysis approach.

reach sufficiently high selectivity. For this reason, InCatT invested in supramolecular ligand technology to get a broad catalyst library that can be applied in asymmetric hydrogenation but is also suitable for many other transition metal catalyzed reactions such as hydroformylation and cross-coupling reactions.

Our library of homogeneous catalysts comprises commercial and in-house made catalysts. The library represents more than 20 structural families of homogeneous catalysts and in total more than 200 commercial catalysts and ligands. The catalysts of our library can be classified according to several criteria:

### Ligands & catalysts:

- Chiral sulfonamide-phosphorus ligands (METAMORPhos family)
- Chiral Ureaphos ligands
- IndoPhos ligands
- SHB (single hydrogen bonded) ligands (ureaphosphine/phosphoramidite)
- Examples of commercially available ligands and ligand families : Josiphos, Walphos, Duphos, DuanPhos, Tangphos, XPhos, JohnPhos, Phosphopin, BenzP\*, QuinoxP\*, SEGPhos, BINAP, XantPhos, MonoPhos, SIPhos, Triphos, PNP pincer ligands, PHOX ligands

# InCatT libraries of catalysts

The power of using supramolecular bidentate ligands lies in the easy synthesis of building blocks and the in situ formation of the catalyst by just mixing with the catalyst precursor, allowing easy combinatorial experimentation. (see fig. 1). We develop automated synthesis protocols for some of the supramolecular ligand building blocks, allowing to diversify the library of supramolecular ligand building blocks (in stock more than 100 analogues) with 32 per day. With this we can generate an extensive library of 100.000 unique catalysts. This method was successfully applied to the asymmetric hydrogenation of several challenging substrates, and world record selectivity was typically achieved within three weeks.

We have also performed screening experiments using commercially available ligands after discussions with clients.

## Heterogeneous catalysts

Heterogeneous catalysts can be powerful for certain conversions, for example in reductive reactions in which no chiral compound is formed. Also heterogeneous catalysts differ in activity and selectivity, depending on the catalyst-type, support, and metal distribution across the surface, and therefore, screening of such catalysts can be important in the optimization of a process.

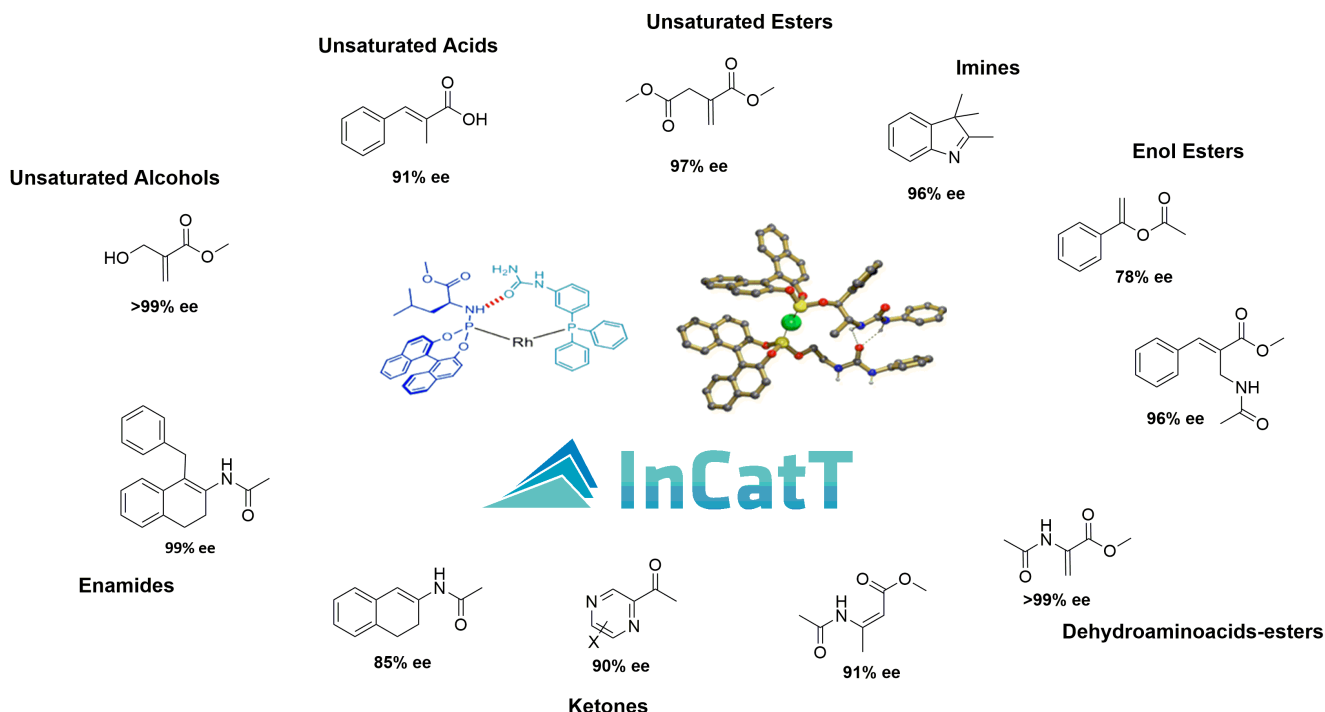
InCatT has more than 80 different heterogeneous catalysts in stock, mostly from known producers to ensure the availability at relevant scale, for screening of hydrogenation reaction, including:

- Reduction of carbon-carbon multiple bonds
- Reduction of carbonyls, nitriles, oximes
- Reduction of esters/carboxylic groups into alcohols
- Reduction of nitro group.
- Reduction of aromatic groups
- Debenzylation

## Conclusion

InCatT has a unique catalyst library consisting of both InCatT's proprietary supramolecular catalysts and extended library commercially available ligands and catalyst systems. Together, with the automated parallel synthesis protocol for the preparation of supramolecular bidentate ligands an unprecedented library of >100.000 unique catalysts is available.

This catalyst library, in combination with InCatT's state-of-the-art high throughput infrastructure allows us to perform >96 reactions per day (using Chemspeed Accelerator) and 32 kinetic experiments per day (using AMTECH SPR16, [see application note](#)) allowing for a fast catalyst lead finding and catalyst optimization.



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