# Fast and Efficient Catalyst Optimization Strategies

## High throughput screening of catalytic reactions using AMTECH SPR16

*A. M. Kluwer, J. Daubignard , X. Caumes, Z. Abiri, J. N. H. Reek*

InCatT B. V., Science Park 904, 1098 XH Amsterdam, The Netherlands

Catalyst research requires specialized knowledge, well-trained scientists and equipment. Within this application letter, InCatT B.V. will provide an overview of the research strategies we have developed for the AMTECH SPR16 reactor system.

## Introduction

InCatT is CRO specialized in catalyst screening and catalyst development from initial catalyst lead finding to process optimization. For this purpose, InCatT employs different reactor systems for High Throughput Experimentation (HTE, 96-well reactor Chemspeed Accelerator), kinetic investigation (AMTECH SPR16), and upscaling to 20 liter batches (Buchi Kiloclave). This application note will highlight InCatT approach using the AMTECH SPR16 platform.

## AMTECH SPR16 Robot Platform

The AMTECH SPR16 is a reaction platform for parallel testing of ***homogeneous*** and ***heterogeneous*** catalytic reactions. The 16 independent reactors can be programmed individually in terms of reaction temperature, pressure and stirring speed allowing to screen a significant reaction space in a single overnight experiment.

The system can be run isobarrically (meaning at constant pressure) at 4 different pressures. For catalytic reactions that consume reactive gas such as hydrogenation, carbonylation, and hydroformylation reactions, the gas-uptake curves will be recorded. Thus in a single overnight experiment the full kinetics of the catalyst system can be obtained. Besides the gas-consumption also the reaction temperature, the pressure, the stirring rate and the gas-uptake curves are recorded for each individual reactor. InCatT uses this platform to:

- Perform catalysts screening to compare different catalysts under well controlled reaction conditions,
- Perform highly detailed kinetic studies,
- Evaluate the catalyst's window of operation (by spiking known impurities),
- Perform DoE studies,
- Prepare small amounts (up to 1-2 grams) of new material.


Fig. 1: Front view of the AMTECH SP16 (Gen 2). .

## Reaction conditions

The reactions in the AMTECH SPR16 can be run under under a wide range of reaction conditions such as:

- Temperature -10 to 200 °C,
- Pressure 5- 150 bars,
- Stirring rate 200 RPM – 2000 RPM.

The AMTECH will flush each reactor with argon before and after the reactions so that the catalyst can be introduced under inert conditions and the product will not degrade after the reaction. In addition, the AMTECH SPR16 also offers the following features:

- Performing reactions below ambient temperature,
- Addition of reagents to the reactors under pressure,

Application Note

# Catalyst Screening Technologies

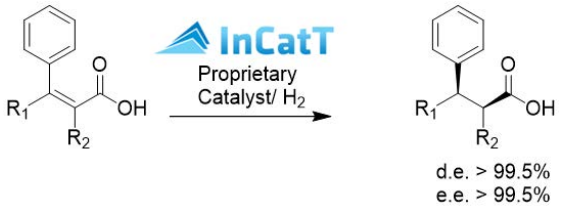
Fig. 2: The AMTECH SPR16 stainless steel reactors (316SS).

- Automatic reaction sampling under reaction conditions (feature available on our AMTECH SPR16 Gen 1 platform)

With our two AMTECH platforms (Figure 1), InCatT can screen large reaction sets evaluating new catalysts and conditions, hereby obtaining highly detailed information for each reaction. In the section below, we describe how InCatT uses its AMTECH infrastructures for catalyst development and optimization studies.

## Catalyst optimization studies

During one of our asymmetric hydrogenation studies, a highly efficient and selective catalyst was developed based on InCatT's proprietary catalyst library (see Scheme 1).




Scheme 1: Asymmetric hydrogenation using proprietary InCatT technology.

After identification of the catalyst lead, the catalyst optimization and process intensification studies were performed. Although the very high chemo- and enantioselectivity were maintained at higher substrate concentration, the productivity dropped significantly (lower yield). A second optimization round was initiated in the AMTECH SPR16 in which various solvents were screened (see Figure 3). After a project of 2 weeks (performing 32 reactions), the recorded gas-uptake curves were analyzed by InCatT's smart optimization procedure and the problem was identified as a substrate/ product inhibition. Changing the solvent from DCM to ethanol the productivity could be increased by a factor 4!

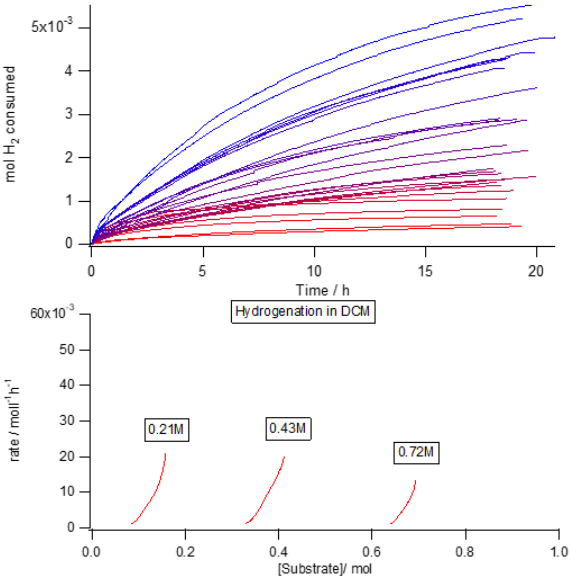



Fig 3: Recorded gas-uptake curve for the catalyst optimization study (top). Kinetic Progress Analysis curve (rate versus [Substrate]) showing considerable substrate and product inhibition.

## DoE-studies in AMTECH SPR16

The design of experiments (DoE) is a statistical approach for the optimization of process. Precious information on the variation of different factors are obtained and with the goal to determine the optimum values to run the process. In this regard, the AMTECH is perfectly suited for DoE study as it allows for the variation of multiple factors for a single set of reactions running simultaneously and therefore reducing considerably the time and cost of development.

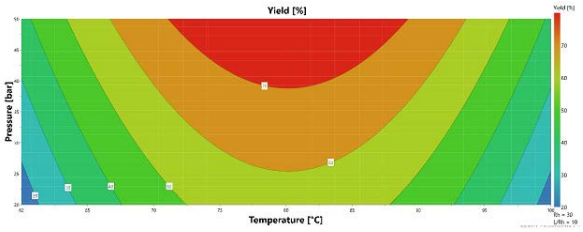



Fig 4: Temperature/ pressure response surface for the yield of product.

In one of our hydroformylation projects, we performed a DoE optimization for a scale-up using 4 factors (resolution IV). By running only 11 experiments in a single run of AMTECH, the DoE indicated that pressure and temperature were the two most important factors. The best conditions were identified at high pressure (50 bars) and intermediate temperature 80 °C (see Figure 4, red part of the response surface).

**InCatT B.V.**
**Science Park 904**
**1098 XH Amsterdam**
**The Netherlands**

Phone: +31 (0)20 525 6490
Web: www.incatt.nl
Info: info@incatt.nl