

RSC Speciality Chemicals Symposium 2009: Catalysts for Change

NanoSelect™ Catalyst Manufacturing Technology Introducing the First Lead-free Replacements for Lindlar catalysts

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The presentation focuses on the novel patented BASF NanoSelect™ manufacturing technology. In detail, the presentation will cover how this innovative technology leads to the development of the world's first lead-free replacements for Lindlar catalysts. In addition, the use of these catalysts, e.g. in the highly selective partial hydrogenation of alkynes to cis-alkenes will be discussed. Concluding, the unique benefits of the NanoSelect catalysts will be highlighted including the significant lower metal content of these catalysts which lead to highly cost effective hydrogenation processes.

Enabling Catalysis in the Pharmaceutical Industry with High Throughput Screening (HTS)

**Garrett Hoge
Solvias, Switzerland**

Homogeneous catalysis, both chiral and achiral, can provide powerful chemical shortcuts that result in short synthetic sequences and low costs of goods for the manufacture of pharmaceuticals. However, as the promise of these catalytic technologies has grown, so have the numbers of industrially viable ligands and catalysts that are available to researchers. A ligand or a catalyst must be discovered from screening among hundreds of

choices to fit to each individual catalytic step. High throughput screening (HTS) as a substitute for classical singleton or parallel reaction techniques provides an advantage to finding leads quickly with little manpower. High throughput screening will be presented as an applied science with critical success factors discussed such as equipment, personnel, ligand/catalyst library, workflow, and know-how. Furthermore, several key examples demonstrating this powerful technique will be discussed with a focus on industrially popular asymmetric hydrogenation and C-N coupling.

From High-Throughput Experimentation (HTE) to High Output Experimentation (HOE): Application to Materials Science.

**Laurent Baumes,
University of Valencia, Spain**

The aim will be to show how HTE can help in catalysis and in formation of compounds. Then, different ways in which HTE has been used will be presented to show how the usability and information retrieval from these experiments can be improved.

Beyond Palladium - The New Iron Age

**Robin Bedford
Bristol University, UK**

Over the last few decades palladium catalysis has formed the bedrock of many important C-C and C-heteroatom bond-forming reactions. However there are major issues with the use of palladium, such as the cost of the metal, the need to remove heavy metal contamination to low ppm levels in pharmaceutical intermediates and the lack of activity shown with challenging substrates such as secondary alkyl halides. Driven in a large part by these concerns, iron-catalysed C-C bond forming processes are currently undergoing a

renaissance. This talk will cover aspects of this rapidly emerging field and in particular will focus on the use of iron catalysis with 'softer' nucleophilic coupling reagents such as aryl-zinc and aryl boron reagents which present particular challenges but also promise substantial rewards.

Going with the Flow - the Evolution from Batch to Continuous Hydrogenation

Gary Kelly
GlaxoSmithKline, Chemical Development,
Tonbridge, United Kingdom

Hydrogenation is a technique widely used in many fields of the pharmaceutical and chemical industry. For low volume products, hydrogenation is typically carried out in batch mode using stirred tank reactors. Within GSK batch hydrogenation process design has evolved into a well understood, structured design methodology which ensures predictable scale-up. Continuous hydrogenation offers additional business benefit when applied to high volume products. The challenge for GSK and their IMPULSE partner CNRS Lyon was to demonstrate a viable continuous hydrogenation capability for high volume production which also managed the catalytic deactivation typically encountered in pharmaceutical hydrogenations.

Through a combination of process development to define optimal catalytic operating conditions and a duty/standby mode of operation with a packed bed reactor it could be conclusively proven that continuous hydrogenation is viable, which opens up this technology for wider application in the pharmaceutical and chemical sector.

Some Illustrations of the Paramount Importance of Catalysis for Rhodia's Sustainable Development

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For many years, Rhodia has been strongly committed to sustainable development in its processes and product development, and has worked on every possible skill or technology

that can help within this respect. Going downstream to technologies while following the twelve principles of Anastas and Warner, catalysis is definitely a key technology for the chemical industry, as 90% of transformations are using catalysts, especially for intermediates manufacture.

In the past years, the strong perturbation on raw materials and energy prices is enhancing this trend as new raw materials could soon compete to the traditional fossil ones, and new (catalytic) routes could be activated or reactivated.

In the presentation, we will focus on some Rhodia industrial catalytic stories illustrating the importance of catalysis as a differentiating technology for sustainability.

In a second part, we will go back to R&D upstream developments illustrating new ways to approach catalyst research.

Some guidelines will be proposed as potential routes for developments.

Organocatalysis - A New Tool for Industry

Karl Anker Jørgensen

Center for Catalysis, Department of Chemistry

Aarhus University, DK-8000 Aarhus C, Denmark

The lecture will give a presentation of the application of organocatalysis for the addition to aldehydes and α,β -unsaturated aldehydes and show the potential of this new field for the construction of chiral building blocks and compounds having important properties in life science.

Enzyme-Catalysis; Easy and Efficient

Pascal Duenkelmann,

Codexis, Germany

During the last decades scientists all over the world identified a vast variety of processes that allow the production of fine chemicals or pharmaceutical ingredients applying biotechnological methods. However, only a few processes are now applied in industry. The reason for this is that most of these bench processes suffer from unsatisfying efficiency. Producing fine chemicals or pharmaceutical ingredients by these syntheses is much more expensive than producing them by usual chemical methods. The fact that the production process is environmentally friendly and therefore expensive might be acceptable for certain compounds. For those fine chemicals that represent building blocks for the chemical or pharmaceutical industry this is a criterion for exclusion.

In many cases the technical issues of these methods result from an insufficient performance of the used biocatalyst. Its bad performance might be caused by a low enzyme stability, a low catalytic activity, a low selectivity, tedious work-up of the reaction broth and so on. Codexis approaches these problems with its enzyme platform technology, which uses a proprietary DNA shuffling process to evolve customized biocatalysts, or "super" enzymes capable of performing chemical processes according to a highly selective set of specifications. This technology creates new and smarter enzymes that improve chemical manufacturing processes. This technology is available for various classes of enzymes like alcohol dehydrogenases, transaminases, hydrolases, etc. Processes based on the application of these optimized enzymes meet requirements regarding economic efficiency (high substrate loading, short reaction time, conversion at ambient temperature, easy work-up) and environmental sustainability at the same time.

Immobilised Bulk Enzymes for Chiral Intermediate and Chiral API Production

Rob Schoevaart

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Enzymes meet the increasing demand by manufacturers of chemicals and pharmaceuticals for enantiomerically pure compounds, because of their greater selectivity and specificity and because of their mild reaction conditions and lower energy consumption. Immobilisation of enzymes offers easier separation and reuse of enzymes thereby making production processes more cost effective. Additionally process conditions can be chosen with increased flexibility.

Despite the impressive progress in asymmetric synthesis, the dominant production method to obtain a single enantiomer in industrial synthesis consists of the resolution of racemates. For kinetic resolutions enzymes are found to be most versatile. Besides lipases the group of proteases are used since in many cases opposite chiral selectivity is found. Since the list of most attractive commercially available (bulk) hydrolytic enzymes is about 100, one can ask what chance there is for a successful process. The answer is simple: the enzyme is but one of the variables in the equation. The combination with clever substrate derivatisation (yielding the same end product) and medium optimisation (including solvent system, temperature, pH, buffer salts, etc.) yields a choice of at least 10,000 - 100,000 distinctively different process conditions with varying yield and enantioselectivity. As a result of these developments, industrial biocatalysis is steadily growing and the ongoing progress will ensure continued success in meeting new industrial challenges. Clearly, enzymatic resolution and enzyme immobilisation have become an indispensable tool in the chemist's chiral toolbox.

Encapsulated Catalysts: Easier, Cleaner, Faster Process Chemistry

Dr Angus Stewart-Liddon
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Transition metal-based catalysis is a key synthetic tool, contributing to an increasing proportion of processes in fine chemical and pharmaceutical manufacturing. Access to complex architectures in fewer steps can be provided by homogeneous catalysts under mild and selective conditions, whilst heterogeneous metal catalysts are routinely employed for reduction and oxidation transformations. The application of such catalysts at scale is not without drawbacks, however, which can include handling issues, 'one time catalyst use', lost metal value and troublesome contamination of product and plant.

The EnCat™ range of polymer encapsulated precious metal catalysts can address these significant issues. In particular, the resultant low level of metal leaching facilitates compliance with regulatory requirements in drug manufacture and avoids often expensive and complex purification operations. Incorporation into a polymer bead also allows for safe, easy to handle and re-useable hydrogenation catalysts which can be used in both batch and flow processes.

The presentation will provide an overview of the EnCat™ technology, with applications of Pd, Pt, Os and Ni EnCat™ catalysts highlighting opportunities for process improvement.

**Catalysis within DSM:
Enabling, Improving, and Changing Chemicals Manufacture**

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Catalytic processes are of vital importance to all business units of DSM: Nutrition, Pharma, Performance Materials and Industrial Chemicals. Catalysis enables chemical reactions that would not occur otherwise. Process improvement is often achieved by improving catalyst performance in terms of chemical and cost efficiency. New developments in the areas of homogeneous, heterogeneous, bio- or organocatalysis not only serve to achieve incremental process improvements, but also initiate step changes ultimately resulting in completely new production methods with lower cost and less waste.

Production processes within DSM Pharmaceutical Products differ from those in other business units in that they typically employ a great diversity of chemical reactions. This diversity is the combined effect of:

- Small production volumes but high prices of a typical pharmaceutical product (allowing technologies not technically and/or economically feasible in other markets)
- The short product lifecycle of many pharmaceutical products (calling for frequent process and technology switches)
- The complex molecular structure of a typical pharmaceutical compound (often requiring enantioselective processes/catalysis).

As a result, all above mentioned forms of catalysis are of interest for DSM Pharmaceutical Products. The lecture will demonstrate various uses of catalysis within DSM and the impact of catalysis on cost and waste reduction. The relevance of catalyst recycling and various ways to achieve this will also be addressed.
