

Successful Scale-Up of Catalytic Processes

PALLADIUM IN INDUSTRIAL CATALYSIS

Reviewed by Chris Mitchell

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A one day meeting on the Successful Scale-Up of Catalytic Processes took place on the 5th October 2006. Organised by the Applied Catalysis Group of the Royal Society of Chemistry (1), it was hosted by Davy Process Technology Ltd (2) at Stockton-on-Tees, U.K. In all, almost 60 delegates attended the meeting, with over 80% being from industry. There were a total of six oral presentations, of which three covered work using platinum group metal (pgm) catalysts, especially palladium.

Cost-Effective Palladium-Catalysed Processes

Ian Archer (Ingenza Ltd, U.K.) described the scale-up of a novel process for the synthesis of pure enantiomers of amino acids and amines. The process uses chemo-enzymatic deracemisation to generate a single enantiomer from a racemic mixture (3). A biocatalysed enantioselective oxidation is used to convert one enantiomer of the amino acid or amine to a non-chiral imine, which is then reduced non-selectively back to the amine, see Scheme I.

In order to develop commercially viable processes, Ingenza have needed to develop cost-effective pgm-catalysed reductions. For example, for the stereoinversion of D-2-aminobutyric acid to

L-2-aminobutyric acid, over 40 different pgm catalysts were screened for use in the reduction step. Initially, a Pd/C catalyst was identified as the most promising candidate, but the cost proved to be too high, even with reuse of the catalyst and recovery of the Pd metal. Development of a second generation Pd catalyst enabled the costs to be reduced to an economically attractive level.

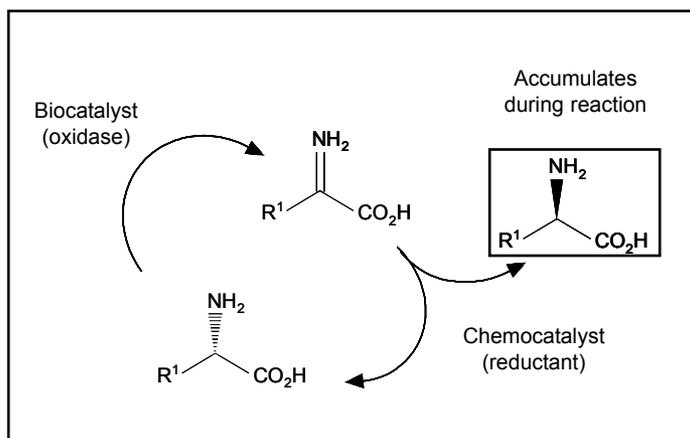
David Johnson (Lucite International Ltd, U.K.) presented a paper which outlined the development and scale-up of their new route to methyl methacrylate (MMA). This novel process employs two catalytic reaction steps:

- carbonylation of ethene in methanol to produce methyl propionate, using a homogeneous palladium-phosphine catalyst;
- condensation of methyl propionate with formaldehyde over a basic heterogeneous catalyst (Cs/SiO₂).

There were several issues which needed to be addressed during the scale-up of the overall process, including product separation and purification issues, catalyst manufacture, and the demonstration of product quality.

Although the initial research had identified a suitable carbonylation catalyst with a turnover

Scheme I Deracemisation of amino acids by a chemo-enzymatic process, using a palladium catalyst as reductant



number of ~ 50,000 and selectivity in excess of 99.9%, the phosphine ligand was not commercially available at that time and the existing synthesis would have been prohibitively expensive. The company therefore had to develop alternative synthesis routes in conjunction with Professor Peter Edwards at Cardiff University, U.K.

In order to achieve recovery of the methyl propionate, the process was designed to operate on the product-rich side of an azeotrope. This had the unfortunate effect of lowering catalyst activity. Further, it was discovered that carbon monoxide poisoned the catalyst; this necessitated operating the process with a high ethene:CO ratio. However, it was then discovered that addition of polyvinylpyrrolidone was able to stabilise the catalyst activity and also improve the Pd recovery.

Optimised Palladium Catalyst Performance

Kevin Treacher (Reaxa Ltd, U.K.) presented an overview of the use of Pd EnCat™ catalysts for organic synthesis. A range of different catalysts are available based on palladium(II) acetate in combination with a variety of phosphine ligands and encapsulated in porous polyurea beads. These catalysts can be used for a variety of synthetic reactions such as Suzuki coupling, Heck reactions and hydrogenations. A catalyst with encapsulated Pd nanoparticles is also available.

A case study of the Suzuki coupling of phenylboronic acid and 4-fluoro-1-bromobenzene to give 4-fluorobiphenyl was presented. Initial screening of different bases in conjunction with a Pd(II) EnCat™ BINAP30 catalyst was carried out in a batch reactor. The best performing system from these tests was then evaluated in three different flow reactor configurations: a continuous stirred tank reactor (CSTR), a tubular reactor and two sequential tubular reactors. With this latter configuration, optimised system productivity in excess of 150 g per g catalyst was achieved; the catalyst still exhibited a stable performance after 250 hours operation.

Other Approaches

In addition to these three presentations which included pgm catalysis, the other talks described the

approaches to catalytic process scale-up used by different companies. Steven Colley (Davy Process Technology Ltd, U.K.) outlined their approach to process scale-up, with the focus being on the use of mini-plants to generate the data required for process design, and the issues that can be encountered. Simon Froom (BP, U.K.) described the scale-up of BP's Avada® process (4) for the manufacture of ethyl acetate from acetic acid and ethene. Professor Wölfgang Holderich (RWTH-Aachen University, Germany) described the development of two new processes: the manufacture of caprolactam *via* the acid-catalysed Beckmann rearrangement of cyclohexanone oxime; and the production of biodegradable lubricants *via* the esterification of natural oils and glycerides.

Conclusion

Overall, the meeting was a resounding success and provided many valuable insights into the varying methodologies which can be used in the scale-up of catalytic processes, whether for more traditional large-scale manufacturing processes or for smaller-scale speciality chemical synthesis. The Applied Catalysis Group of the Royal Society of Chemistry plans to hold a one-day symposium on the Challenges in Catalysis for Pharmaceuticals and Fine Chemicals at the Society of Chemical Industry, London, U.K., on 6th November 2007 (1).

References

- 1 RSC Applied Catalysis Group:
<http://www.rsc.org/Membership/Networking/InterestGroups/catalysis/>
- 2 Davy Process Technology Ltd:
<http://www.davyprotech.com/>
- 3 I. Fotheringham, I. Archer, R. Carr, R. Speight and N. J. Turner, *Biochem. Soc. Trans.*, 2006, 34, (2), 287
- 4 B. Harrison, *Platinum Metals Rev.*, 2001, 45, (1), 12

The Reviewer



Chris Mitchell is the Catalytic Chemistry Expert for Huntsman Polyurethanes and works within their Global Technology organisation, based in Belgium. His main focus is the development of heterogeneous catalytic processes, including hydrogenations, acid catalysis and epoxidations/oxidations. He has particular interests in the characterisation of catalysts, reaction kinetics and catalyst deactivation. Among the platinum group metals, he has worked with platinum, palladium and ruthenium.