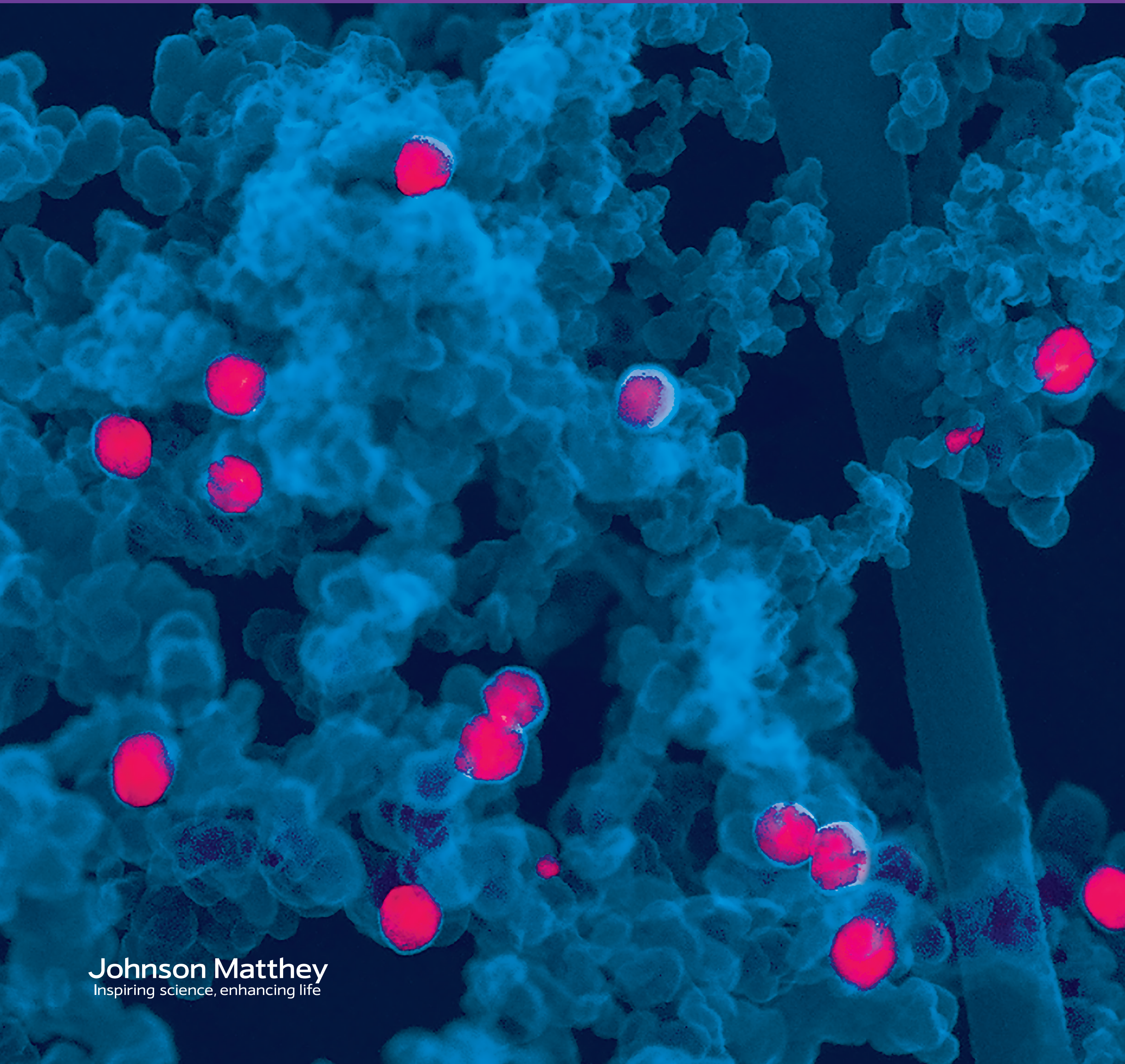
JM

White paper

Optimising chemistry performance through heterogeneous catalyst design



Johnson Matthey
Inspiring science, enhancing life

Dr Danny Mortimer

Global Technical Service Leader
Johnson Matthey

Danny studied at the University of York, UK, completing his MChem degree in 2007. This was followed by a GSK-funded PhD in organic chemistry completed in 2011 at the University of Sheffield. He subsequently spent a year at Argenta and Biofocus as a Medicinal Chemist.

In 2012, Danny joined Johnson Matthey as a Research Chemist for the development of new heterogeneous catalysts, working as part of a research team that combines organic chemistry evaluation for the design, preparation, development and commercialisation of supported platinum group metal catalyst powders. He has single authored a granted patent and recently co-authored a publication on catalyst cost contribution. Subsequently, in his role as Product Specialist for Johnson Matthey's heterogeneous catalysis portfolio, Danny interfaced with R&D, Production, Quality and Commercial to support new business development.

Danny's current role as Global Technical Service Leader investigates the application of PGM heterogeneous catalysts for use in fixed bed and slurry reactors for fine chemical industry applications.

His expertise in the development of new supported PGM catalysts and optimisation of heterogeneous catalytic processes has led to significantly improved value and catalyst performance for customer processes.

How Johnson Matthey can work with you

Johnson Matthey (JM) is committed to building strong relationships by providing a flexible approach that meets the specific needs of our customers. With our strong reputation for reliable supply, global manufacturing capability, metal precursor supply with closed loop supply through precious metal refining, we can streamline your catalytic processes to maximise value by:

- Providing expert insight in identifying optimal catalysts for your processes
- Performing parallel screening experimentation to assist in defining optimum process parameters
- Optimising unit operations for catalytic steps, improved catalyst mileage, reduced metal inventory and improved impurity profile

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Heterogeneous catalytic hydrogenation for fine chemicals

Chemical catalysis by platinum group metal (PGM) based materials is an essential synthetic technology for the fine chemical industry. Catalysis enables the acceleration of the reaction rate using a substance that itself is not consumed. This allows the production of target molecules to be both efficient and economically viable. To this end, the application of heterogeneous catalytic hydrogenation is one of the most important transformations in the field. In particular, for the fine chemical sector, it is the most applicable method to perform reductions of organic compounds and is a commonly used tool in the synthesis of active pharmaceutical ingredients (APIs).

Heterogeneous catalysts can be described as 'supported' where the catalytically active metal is immobilised on a porous support particle that acts as a carrier. Solid heterogeneous PGM catalysts are employed in a different phase to the reactants and are routinely used to carry out liquid phase hydrogenations (hydrogen gas– liquid – solid) in a batch reactor setup (Figure 1). A catalyst powder slurried with liquid phase reactants in a batch or continuous process can be easily separated at the end of the reaction by filtration. Alternatively, catalyst particulates can be used in a fixed bed reactor setup, through which reactants pass in the gas or liquid phase.

To ensure optimal processes, catalyst design is of paramount importance.

This white paper will cover the various elements that are critical to consider when selecting a PGM heterogeneous catalyst for your process.

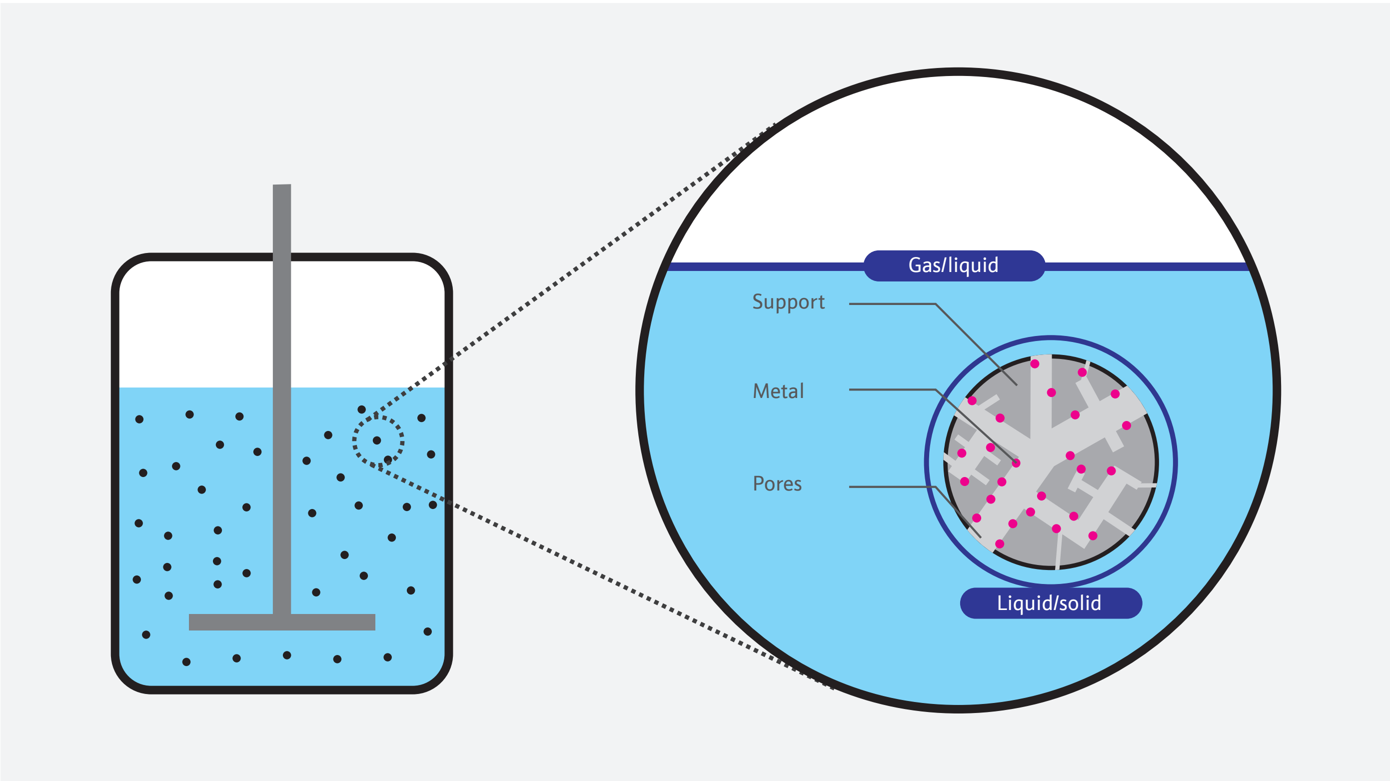

Figure 1. *Heterogeneous catalyst; metal supported in porous particulate*

Optimising chemistry performance through catalyst design

To obtain successful identification and implementation of a catalytic process using PGM based heterogeneous catalysts, many factors should be considered and examined (Figure 2). Both the support material and metal choice are essential to catalytic activity and can be fine-tuned to optimise the reaction output performance.

The desirable performance properties of a catalyst are for it to deliver high reaction activity, product selectivity, recyclability and fast filtration. Achieving this allows for fast reaction rates, lower catalyst loadings and maximised product yield. This ultimately leads to a minimised catalyst cost contribution. The design of the catalyst and choosing the right components are critical to achieving this.

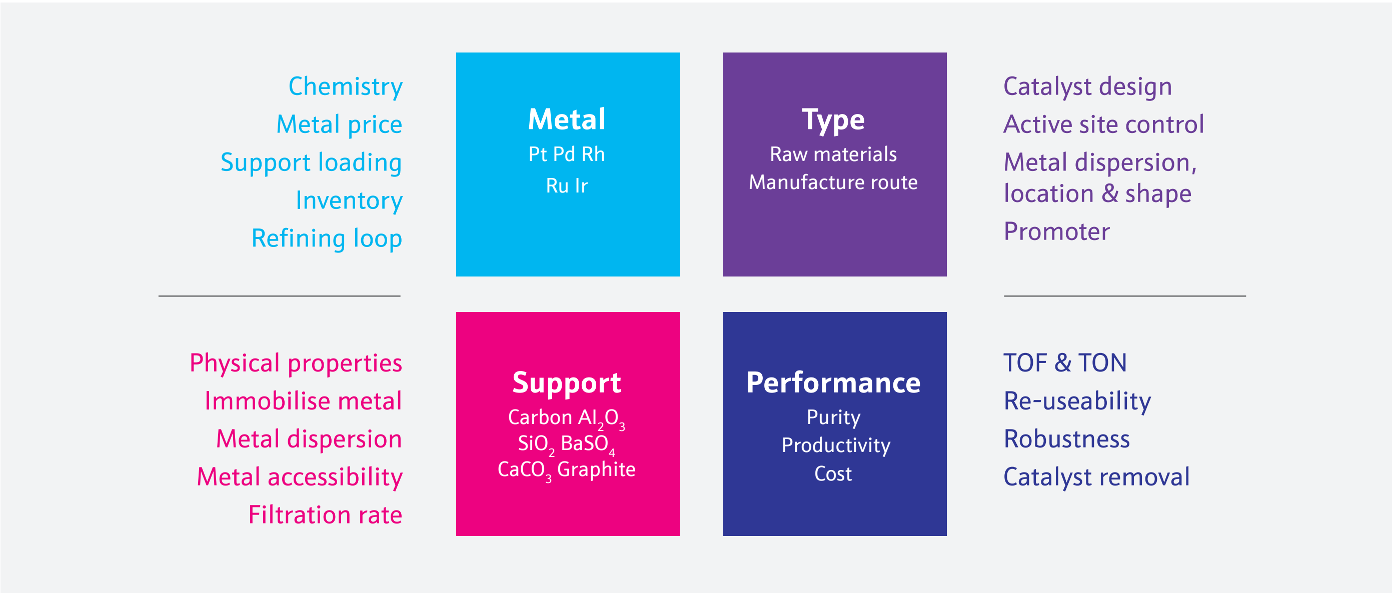

__Figure 2.__ Design factors that impact catalyst performance

Heterogeneous catalysts are continuously being optimised to develop more selective reactions with the catalyst tailored to the activity required by the reaction. With the increasing complexity of APIs, a catalyst must be capable of performing a selective hydrogenation in the presence of multiple other functional groups. By applying the extensive guidance and research from our experts, the most appropriate catalyst for each specific reaction transformation can be identified as illustrated below (Figure 3).

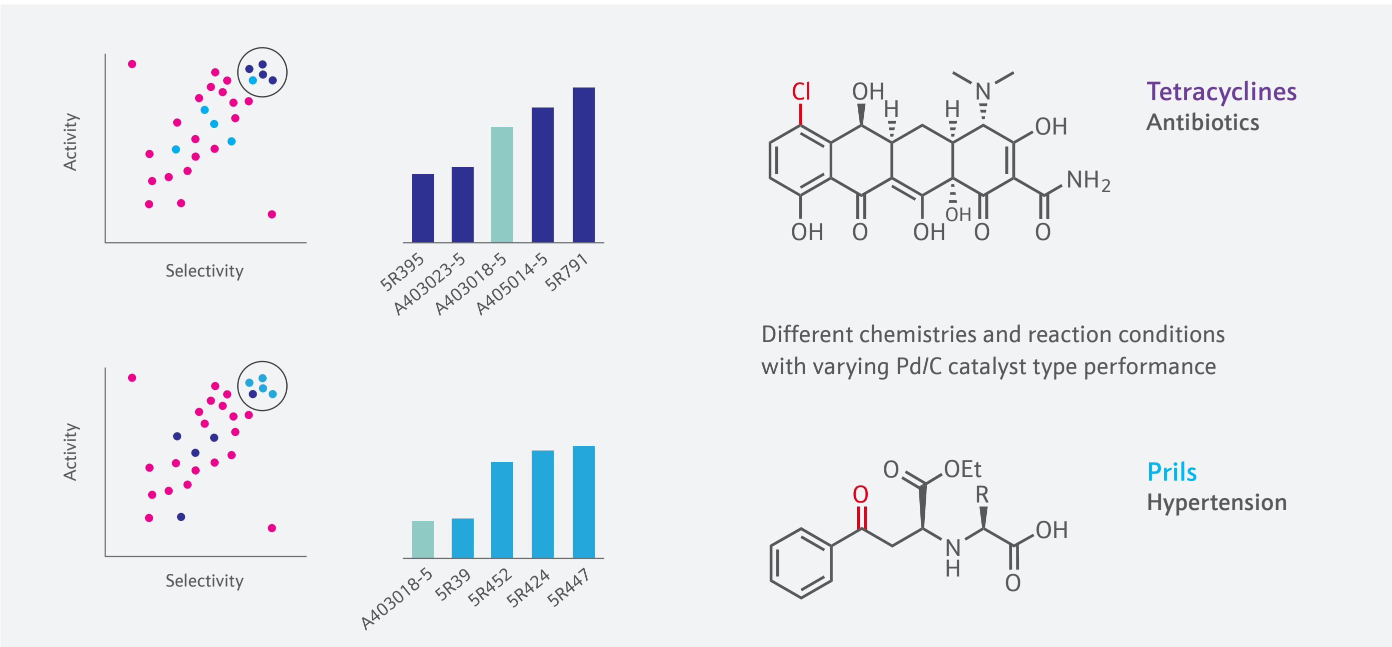

__Figure 3.__ Catalyst type performance differentiation

Choosing the right components

Platinum group metal choice

A metal is chosen based both on its ability to complete the desired reaction and its ability not to perform unwanted side reactions. Choosing the appropriate metal relies on knowledge-based performance for the desired transformation. Palladium is the most versatile of the PGMs for hydrogenation and hydrogenolysis reactions.

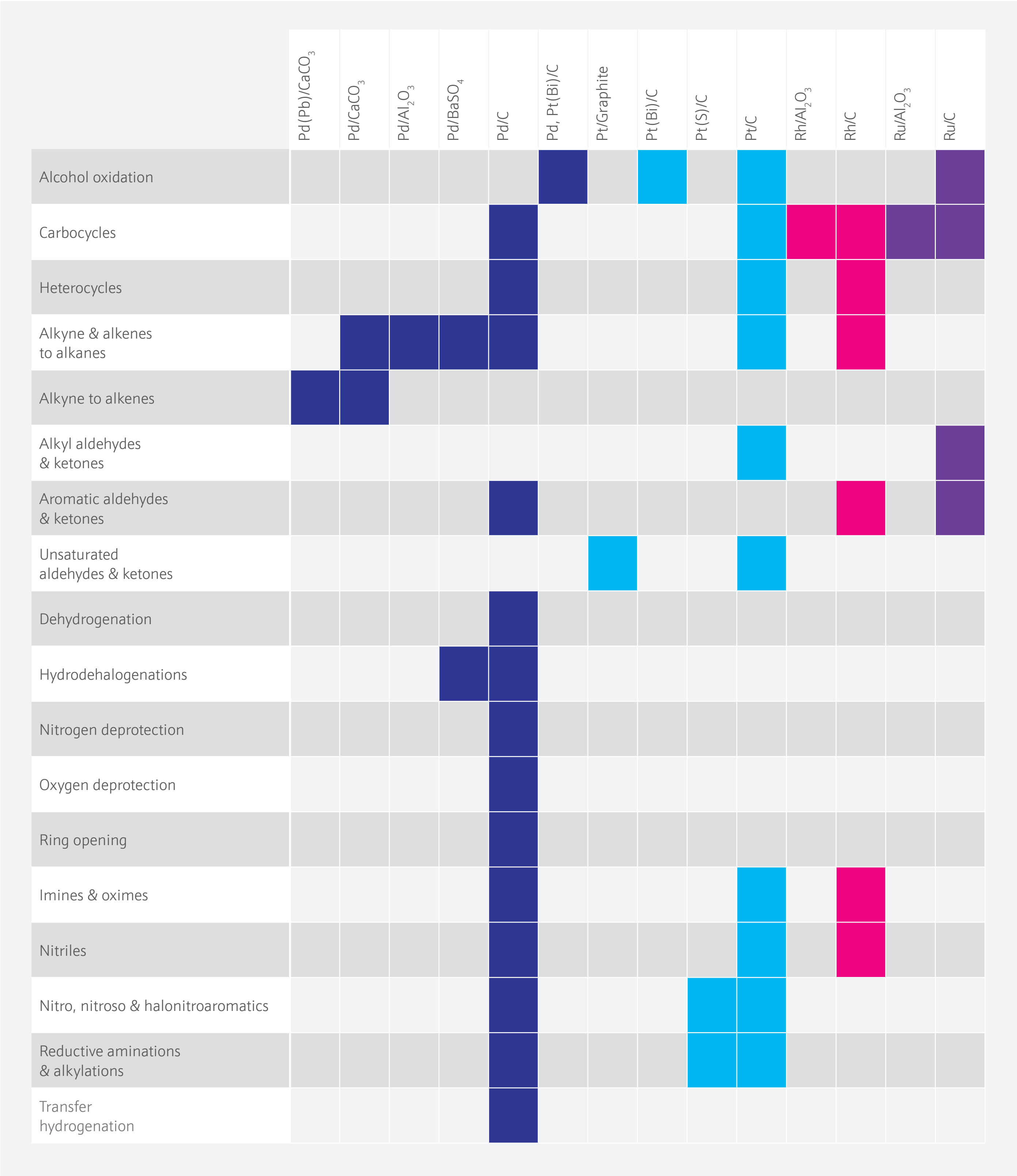

Figure 4. *Different recommended supported metal catalysts per type of hydrogenation*

Catalyst support

The second major component is the support material that the metal is carried on. The main functions of the support are to improve metal dispersion (surface area), activity and durability. When supported on a high surface area carrier, the catalytic metal is present in the form of discrete crystallites (typically a few nanometres in size) which give a very high catalyst activity area per unit weight of metal. For batch reactions, powdered supports are invariably used, slurried with liquid phase reactants.

The catalyst is separated by filtration after reaction completion. A well-designed powder catalyst will exhibit high attrition resistance (to reduce catalyst losses by fines generation) and good suspension characteristics (to resist mass transfer effects). Thus, catalyst supports are selected to incorporate a compromise of properties to generate catalysts of fast filtration with high activity and selectivity.

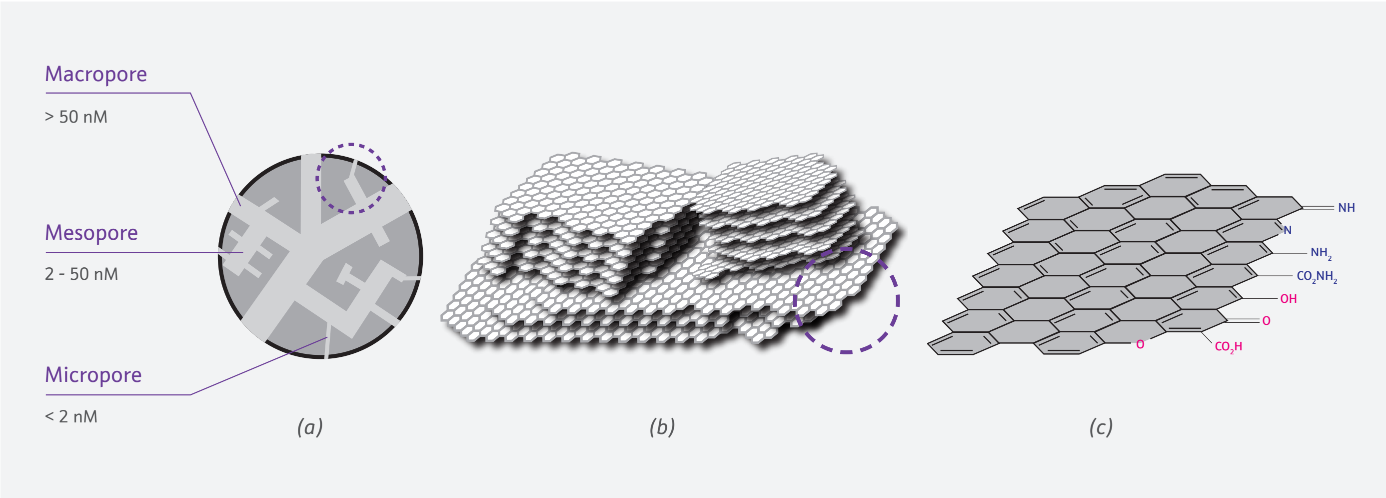

Figure 5*. (a) Pore sizes in support particulate (b) Activated carbon has disordered graphitic sheet structure (c) Graphitic sheet edges functionality type range*

In batch hydrogenation reactions, activated carbon is the predominant choice of highly porous support for powdered PGM catalysts. The chosen activated carbon type can have a significant effect on catalyst performance. As activated carbon is derived from naturally occurring raw materials, there are many variations and grades, with each type having its own physical properties and chemical composition. These properties are functions of particle size and shape, pore volume, pore size range, surface area, activation procedure and material base. The pore structure of the activated carbon may modify the role of the metal since the course of a reaction is often greatly influenced by the rates of diffusion of reactants and products within the catalyst pores.

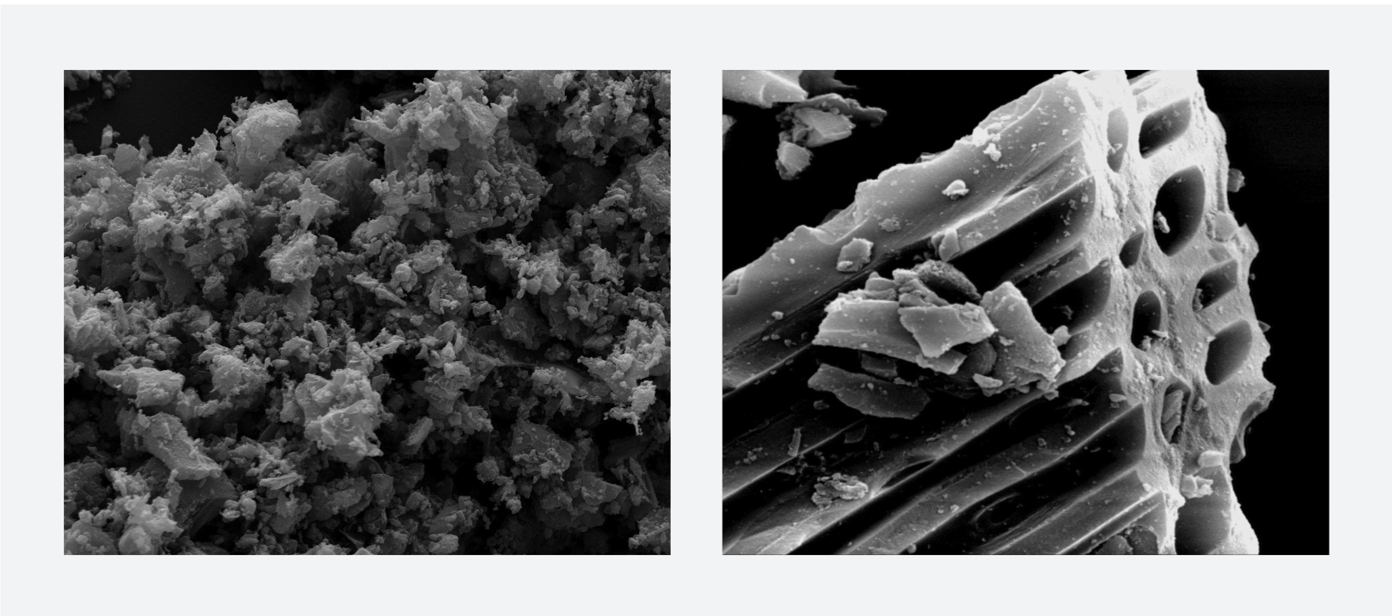

Figure 6. *SEM images of different carbon grades used in JM catalysts*

Manufacturing method: choosing the optimal combination

Metal dispersion / shape

Finally, the most important factor is how the catalyst is manufactured. Recipe and design knowledge and industry know-how are key for catalyst performance. This is typically designated by a type of code assigned by the catalyst suppliers, which means no two catalysts types are identical. Catalyst performance can be altered significantly by the appropriate choice of support material, metal location and dispersion within the pore structure of the support. Considerable progress has been made for the development and application of new catalysts.

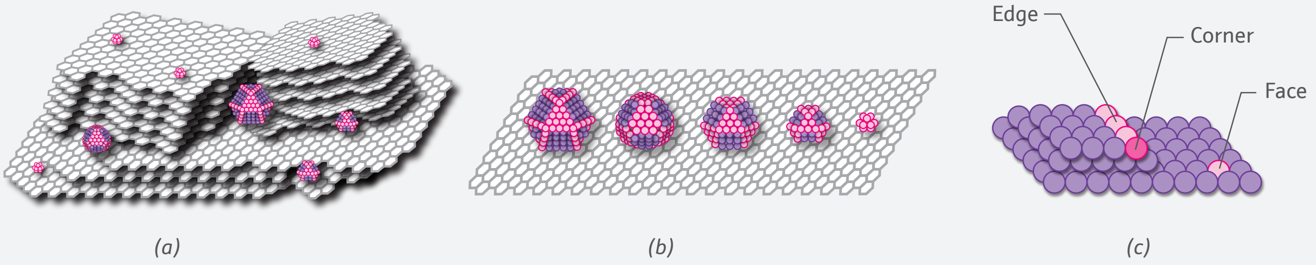

Figure 7. *(a) Support and metal interaction (b) Metal dispersion and shape (c) Metal atom*

When considering the metal choice itself, the chemical transformation takes place on the metal surface and the inherent electronic properties of the metal affects the ability to conduct catalysis.

Below illustrates different examples where metal location and dispersion changes with respect to the support particulate for JM PGM supported catalysts (Figure 8).

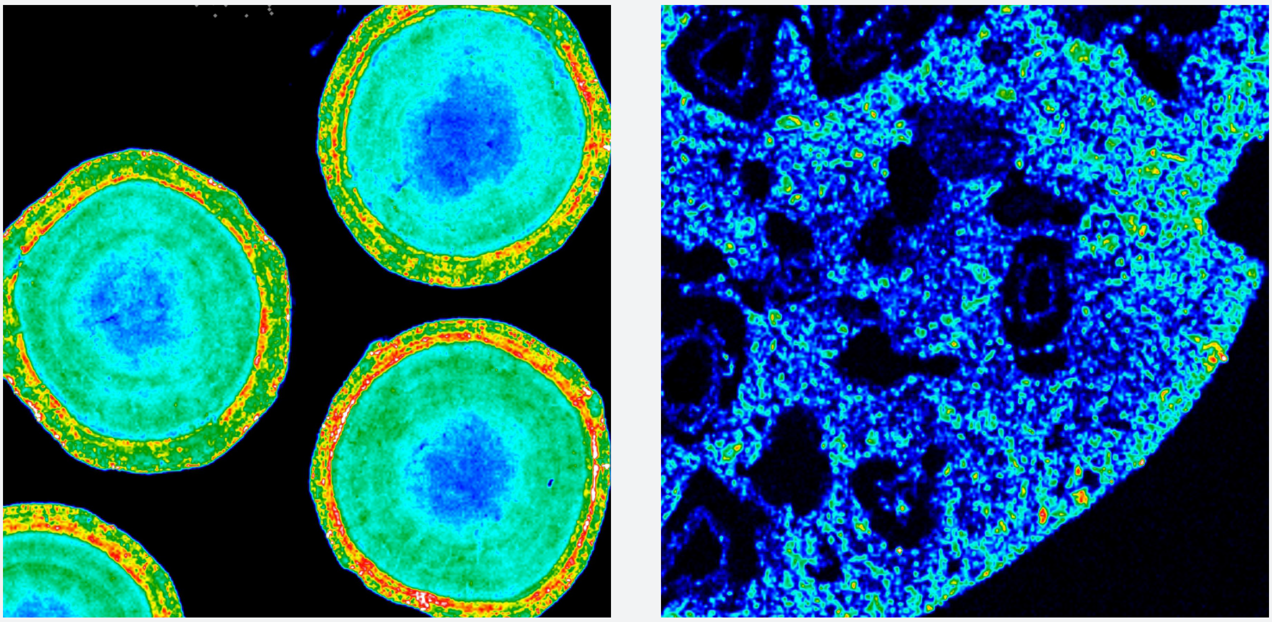

Figure 8. *EPMA images of JM PGM supported catalysts*

Metal location

Johnson Matthey has developed techniques to deposit the metal selectively in the desired location with respect to depth in the carbon particulate pores. The catalysts are designed with different metal locations for reactions performed under different conditions of hydrogen pressure and temperature (Figure 9). Eggshell catalysts (metal located on the exterior surface of the support) would be chosen for high activity at low hydrogen pressure. Uniform catalysts (metal evenly dispersed throughout the support structure) exhibit greater activity at high hydrogen pressure. The location of catalytic metal deep into the support may lead to large in–pore diffusion resistance to reactants. This will result in increases in residence time and possible changes in reaction selectivity. Thus, the variation of the metal location can be used to adjust the activity and selectivity of the catalyst.

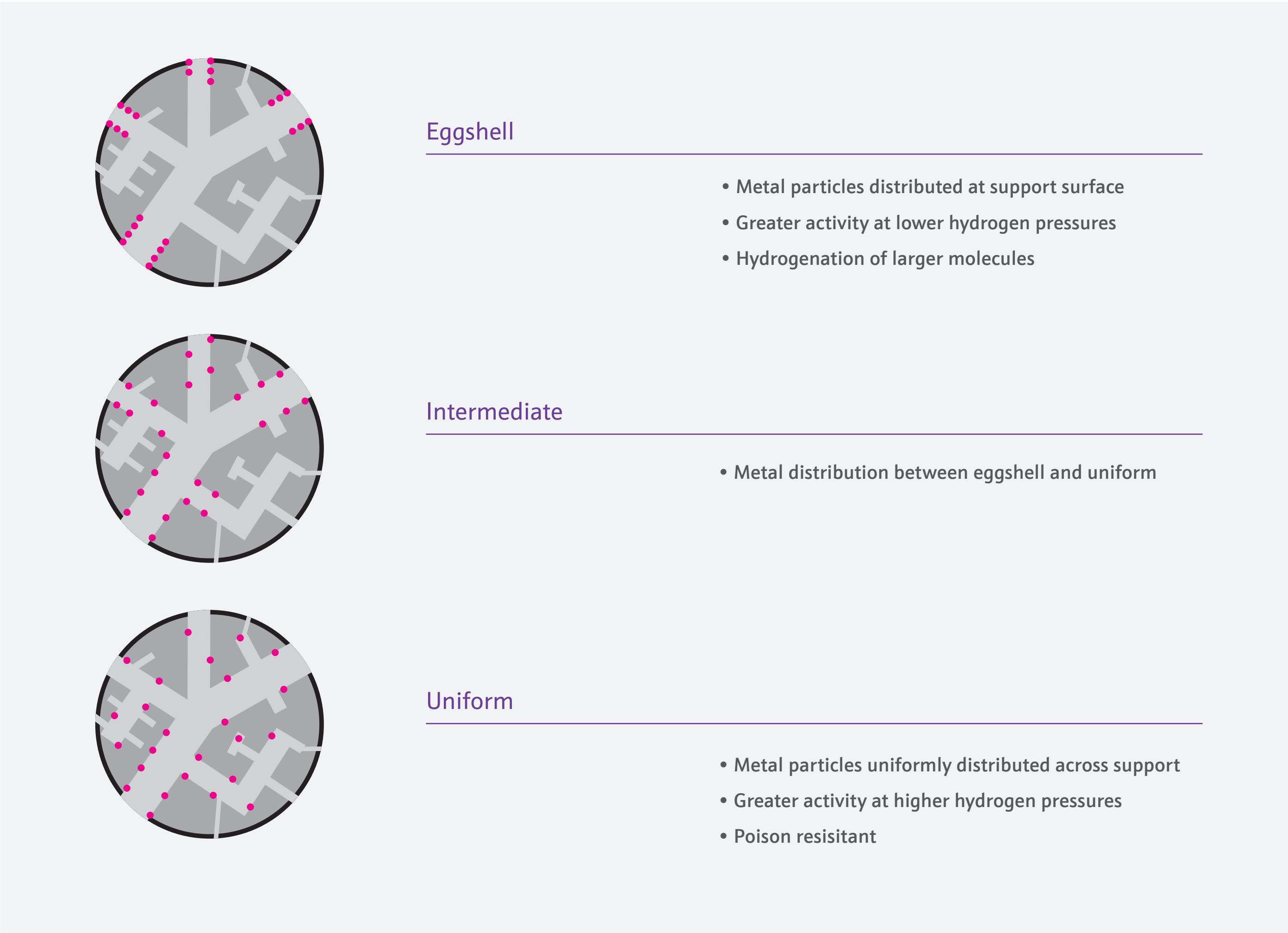

Figure 9. *Different metal pore depth location*

Final product

Catalyst performance for customer processes is sensitive to the metal, support properties and preparation method. They can be designed for optimal selectivity, recyclability, activity, stability and or to minimise metal cost contribution. Examples of finished commercial Pd/C catalysts are illustrated below, showing control right down to the metal active site (Figure 10). Guidance from the JM experts regarding the most appropriate catalyst type for each specific reaction transformation can bring significantly increased value to a process. Our heterogeneous catalyst offering is continuously being optimised to develop more selective reactions with the catalyst tailored to the activity required by the reaction.

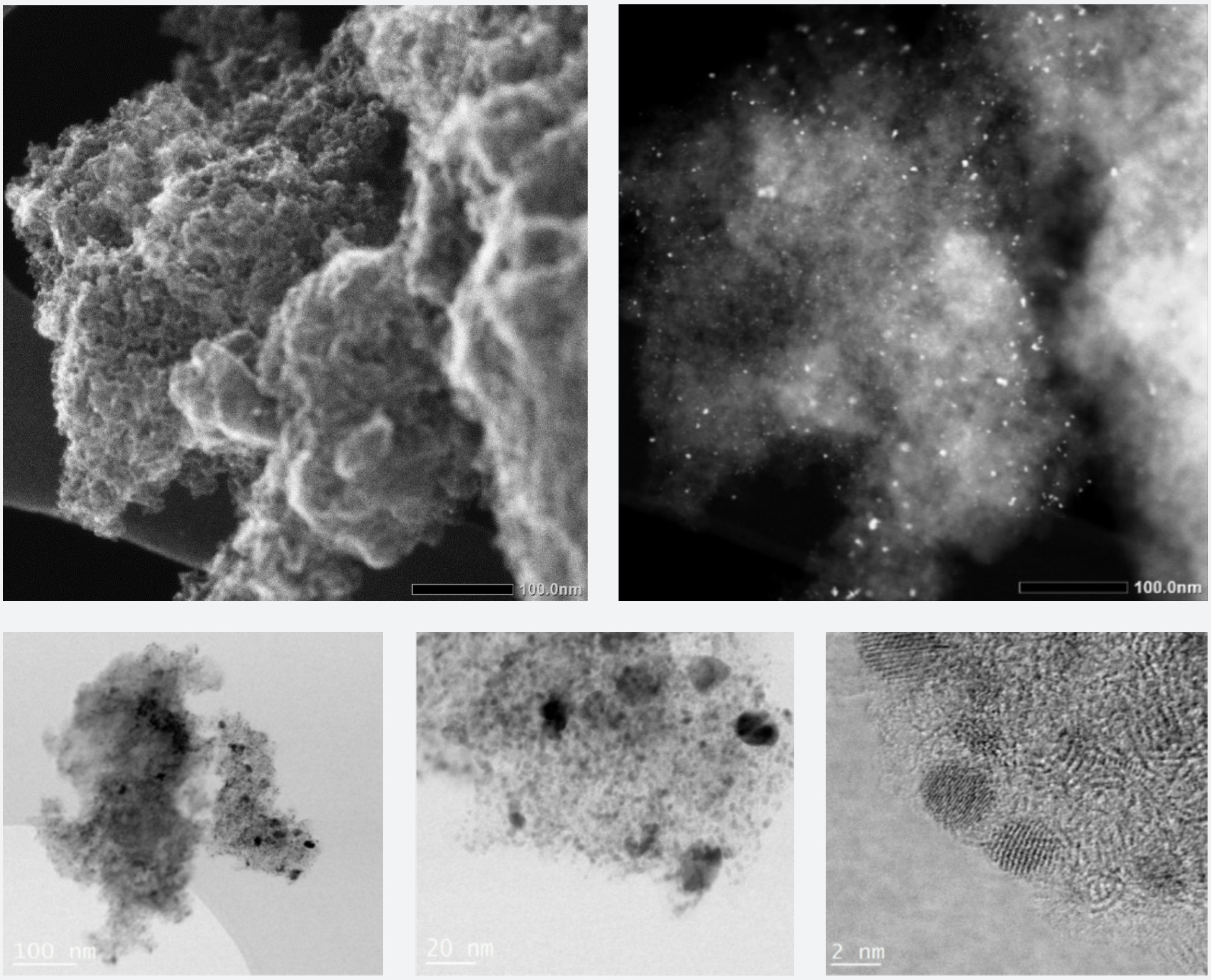

Figure 10. *SEM images of JM PGM supported powdered catalysts*

Case study: Recyclable Pd/C for the Prils

Recent successful catalyst design has been applied to a series of Pd/C catalysts for the optimised manufacture of the blockbuster class of drugs known as the Prils. The Prils are Angiotensin - converting enzyme (ACE) inhibitors that are used to treat hypertension. The main construction route of the Prils framework involves a catalytic benzylic carbonyl reduction to remove the ketone. With the increasing cost of Pd, minimising the contribution towards the Prils manufacture from catalyst use is key. Therefore, the design of catalyst performance was optimised for fast filtration without fines loss and recyclability while maintaining a high proportion of the original activity. These catalysts provide high product yields keeping by-product formation to a minimum and exhibit excellent recyclability.

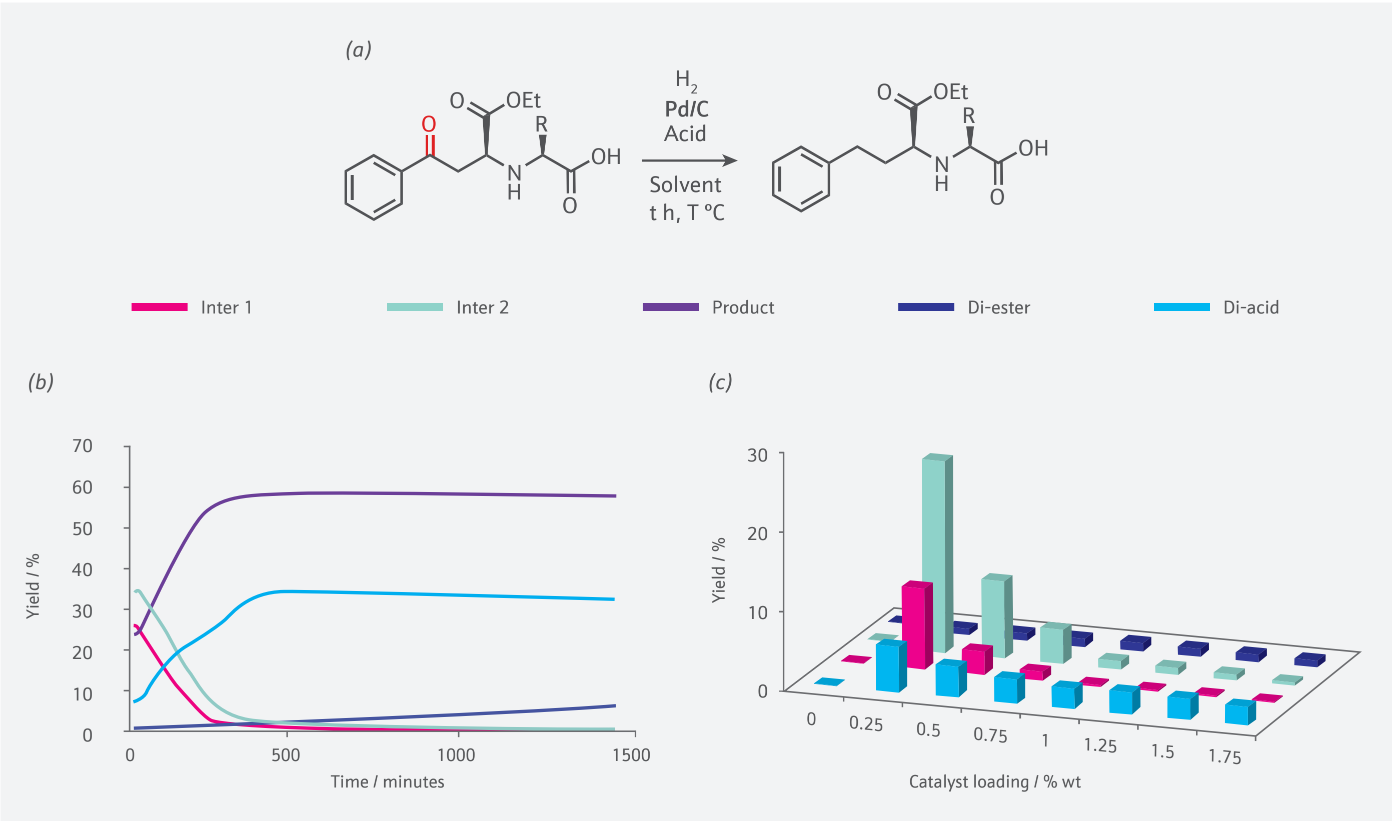

Figure 11. *(a) Pd/C ketone hydrogenolysis synthetic strategy for the Prils (b) Reaction profile indicating intermediate lifetime key to byproduct formation (c) Catalyst loading also linked to selectivity*

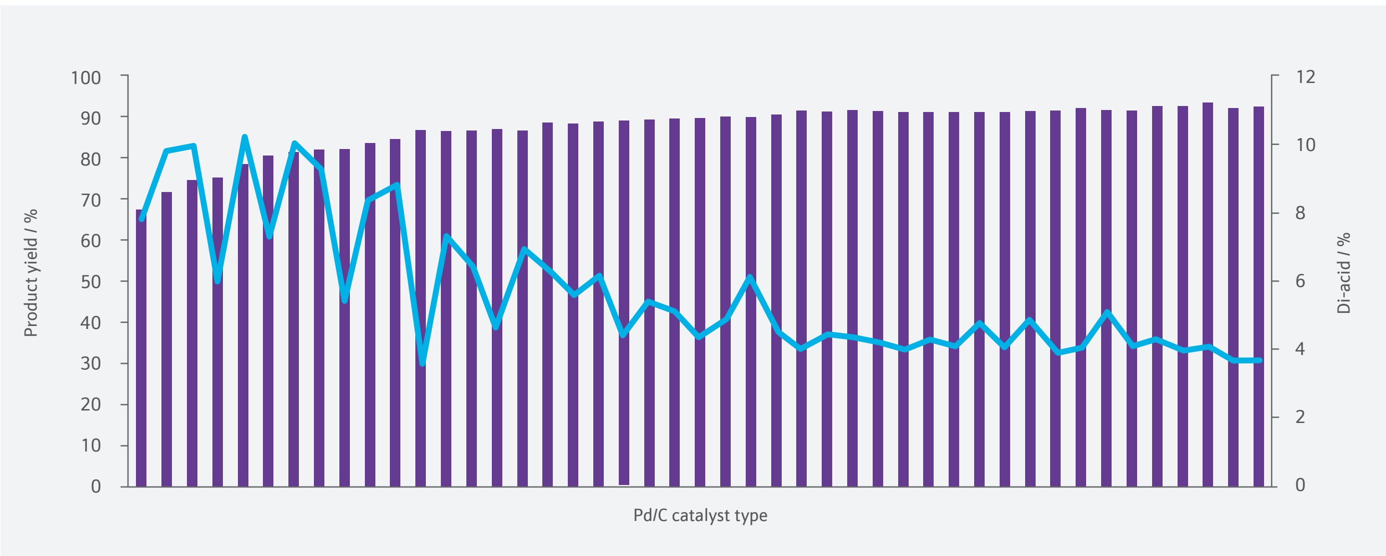

Figure 12. *Catalyst ranking*

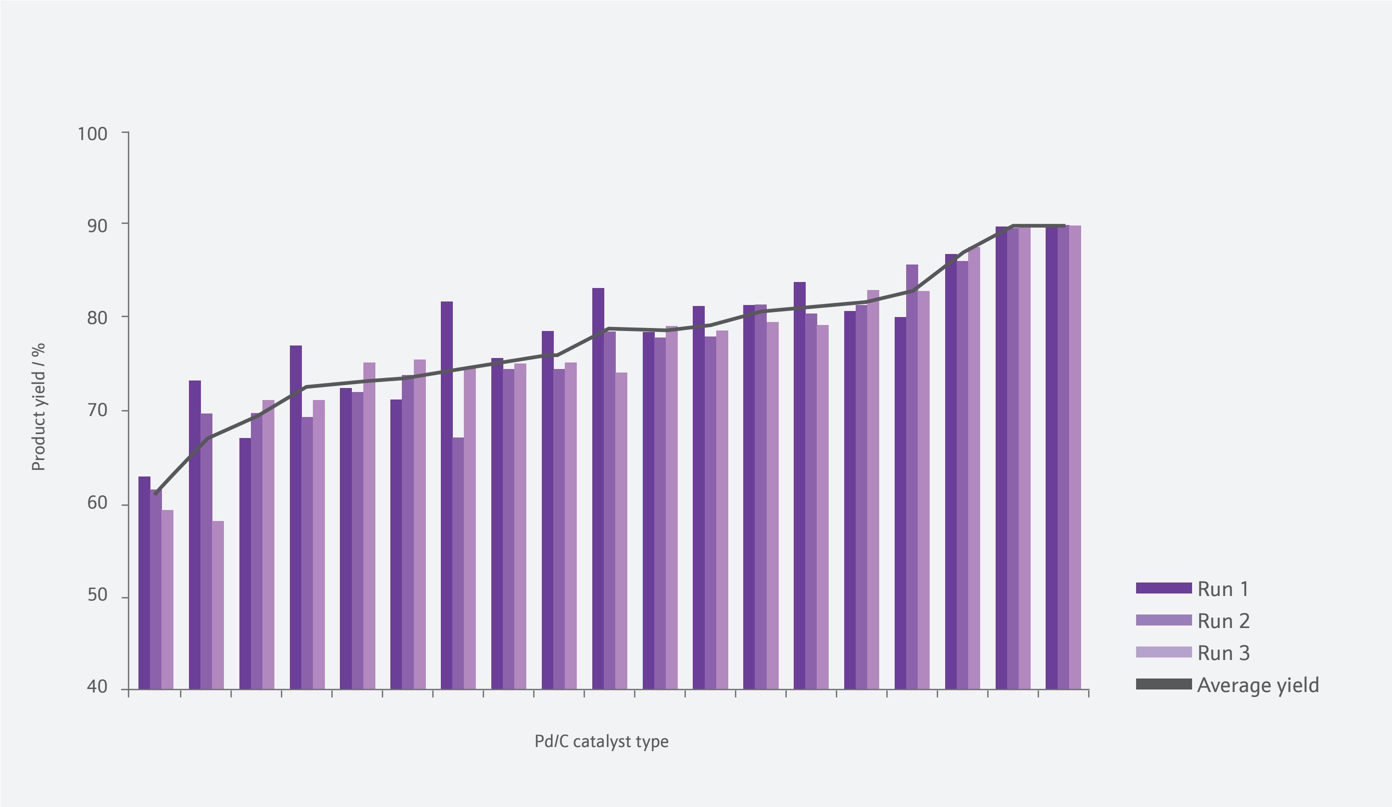

Figure 13. *Catalyst reusability ranking*

Summary

Although a relatively mature technology, over the years, the use of heterogeneous catalysts has garnered a somewhat undeserved dated image in the industry. The technology is synonymous with scale-up and is a reliable and efficient method of performing many important chemical transformations that are essential to the fine chemical industry.

With the increasing complexity of substrates and increased catalyst performance demand, hydrogenations in the presence of multiple functional groups pose increased difficulty. New catalysts are being developed that can reduce specific functional groups in the presence of previously problematic groups.

As is true with most industrial processes, experience and expertise in handling catalytic reactions are essential to optimising reaction conditions and choosing the ideal catalyst type. Every industrial reaction has varying requirements that must be evaluated on a case-by-case basis.

Johnson Matthey provides an essential service in terms of both catalysts supply and supporting optimal catalyst identification through in-house parallel screening experimentation and or expert recommendations.

Whether you are looking for an existing catalyst, customised solution, or to improve an existing process, our highly accessible support team is ready to work with you. We are committed to providing our customers with the best technology for optimising catalytic processes and for minimising the catalyst cost contribution factor.

For more information visit matthey.com/hetcat
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Published November 2021