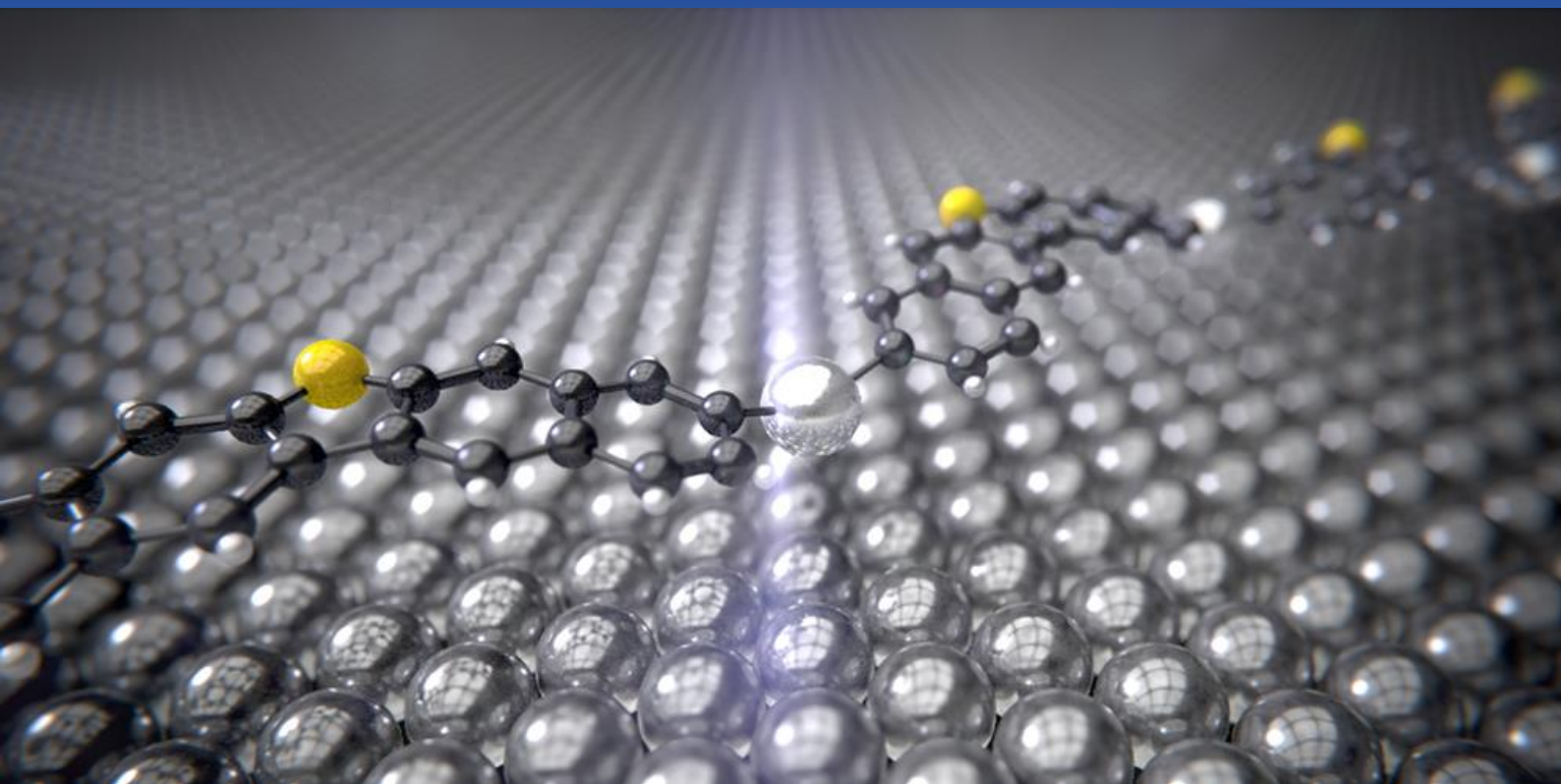


# Heterogeneous Catalysts

## Enabling a Selective Continuous Hydrogenation Process

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Continuous hydrogenation is realized in PharmaBlock by using micropacked reactor, in which heterogeneous solid substrate supported catalysts are filled. The majority of the catalysts are designed, developed and manufactured in-house. In some cases, PharmaBlock tailor-makes customized catalysts on top of the in-house catalyst catalog, in order to fulfill the specified requirements. Among many, low selectivity of a hydrogenation process is detrimental to quality of drug substances and related intermediates.

### Case study: An optimized catalytic solution for selective hydrogenation

The starting compound is an RSM and not cheap, thus it demands a reliable and economic process to deliver the hydrogenated product. Upon batch process research, it turns out that selectivity and reactivity are trade-off. In other words, catalysts in batch process can achieve mediocre outcome, i.e. poor selectivity, low isolated yield and high cost (both material and production costs). And also the batch catalyst was used in 100 wt%, casting an unacceptable cost pressure. The selectivity issue in this case involves halogen hydrogenolysis and nitro hydrogenation (including incomplete hydrogenation resulting hydroxylamine). The PharmaBlock team turned to continuous hydrogenation, and screened the in-house catalysts.

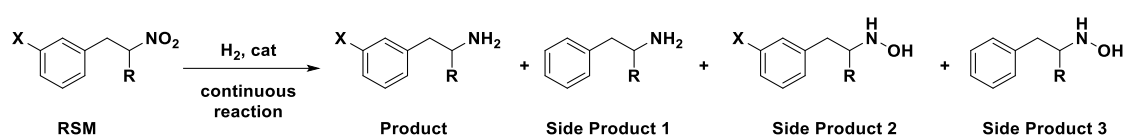


Figure 1. Reaction scheme of a selective continuous hydrogenation process

In the initial screening, we located a 2% Pd based catalyst bearing very high reactivity but poor selectivity, and it serves as a good starting point to improve the selectivity. Thus we started tailor-design R&D. Thanks to our established experience in multi-metallic doping strategy, a second metal dopant is quickly (in just one week) identified to benefit the selectivity issue. Then a finely-tuned catalyst manufacturing was developed, of which the reliability and consistency were focused upon. The new catalyst together with our continuous hydrogenation process lowered the three major side products (in above scheme) to less than 3.0 % in combination, facilitating the downstream purification and dramatically lowered the total cost.

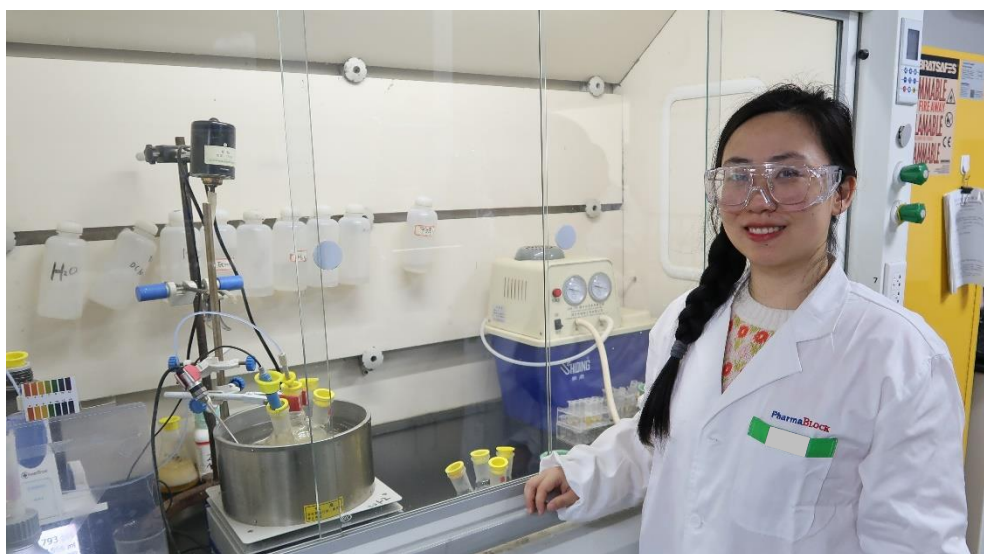


## What makes PharmaBlock unique?

The R&D team at PharmaBlock has extensive heterogeneous catalyst development experience. This team is not only developing catalysts to satisfy customer's projects, but also willingly devotes a lot of effort screening or generating cheaper and yet more efficient catalysts to upgrade our building blocks manufacturing processes, thereby speeding up the delivery of our catalog products and reducing prices, saving both cost and time for customers.



- Pharmablock maintains a heterogeneous solid substrate supported hydrogenation catalyst catalog containing over 300 species. This catalog is able to support quick screening and timely development of a fit-for-purpose process.
- PharmaBlock tailor develops customized catalyst starting from a catalog catalyst. In case a specific catalytic performance is desired, a systematic development project can be conducted, with the aid of various material science analytical methods.
- PharmaBlock's catalysis research constantly converges with process chemistry, CMC research, and manufacturing expertise. In this way, the catalysts developed are well suited for the entire drug development project. In fact, our catalyst researchers are also continuous hydrogenation process engineers.



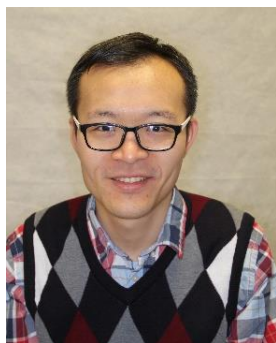
## A glimpse into the future

Catalyst is the key to overall better process performance including reactivity, selectivity, cost, safety and environmental benefits.

PharmaBlock is looking forward to expanding its hydrogenation catalyst catalog and strengthening its capability of catalyst development. Meanwhile, the team will also build up the experience in other areas of heterogeneous catalysts by taking advantage of the proven strategy.

## About Author

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