

# Apeiron's Metal Scavenging Solutions

## Metal scavenging solutions

Apeiron Synthesis is dedicated to providing transformative products and services to enable our customers to save time and money with cost-effective, efficient, sustainable synthetic processes for producing complex molecules. We endeavor to provide solutions that fully realize the powerful potential of olefin metathesis with efficient and cost-effective pathways for commercial manufacturing processes. Our chemistries have applications across a wide range of industries, including: agrichemicals, fine chemicals, flavor and fragrances, polymers and Pharma/Biopharma. Our ongoing internal research efforts enable us to address the specific challenges that each industry may bring.

In addition, we have expanded our toolbox by developing a new line of metal scavengers, for use in R&D and process chemistry applications, to efficiently remove residual catalyst in process.

### Example:

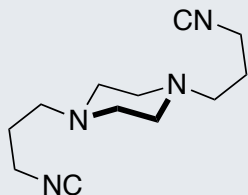
Pharma customers have a need to achieve a low metal content in the final product – often as low as single digit ppm levels.



### Apeiron's solution:

To meet diverse process needs, we've developed two unique, catalyst product lines:

- Solid-supported catalysts – for heterogeneous use or for easy removal by filtration.
- Self-scavenging metathesis catalysts – facile removal in work-up (< 5 ppm residual Ru).



# SnatchCat

ASI033 PCT/EP2014/406739

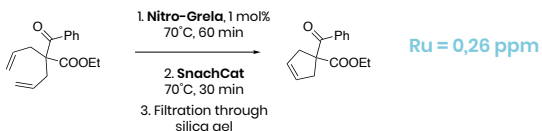
- High efficiency:  
Ru/Pd/Cu content < 10 ppm.
- Fast acting:  
30 min scavenging time.
- Immediate reaction quencher.
- Compatible with broad range of functional groups and solvents.
- Simple workup:  
flash silica gel filtration.
- Facile handling - stable, non-toxic, non-volatile, odor-free.

## Reaction quenchers/ metal scavengers

Metal salts and metal complexes used in many reactions leave traces that affect product quality and can falsify biological screening. Metal scavengers developed at Apeiron are a universal solution for metal removal.

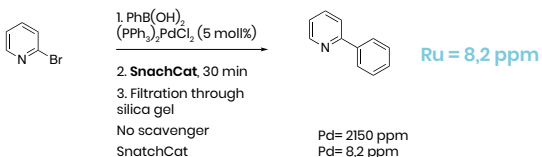
### case study

ruthenium scavenging after ring closing metathesis removal



### case study

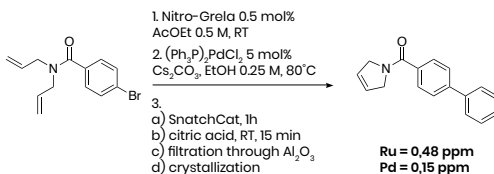
palladium removal after Suzuki coupling



References: G. Szczepaniak, K. Urbaniak, C. Wierzbicka, K. Kosiński, K. Skowerski, K. Grela; High performance isocyanide scavengers use in lowwastepurification of olefin metathesis products; ChemSusChem 8, 4139-4148, (2015)

### case study

removal of ruthenium and palladium products from telescope RCM/Suzuki-Miyaura sequence

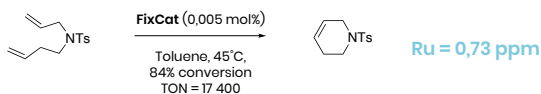


References: G. Szczepaniak, A. Ruszczyńska, K. Kosiński, E. Bulska, K. Grela; Highly efficient and time economical purification of olefin metathesis from metal residus using an isocyanide scavenger DOI:10.1039/c7gc03324a

# Solid-supported Catalyst

Advantages of solid-supported reagents have long been recognized and applied extensively to enable metal removal with simple filtration techniques. Apeiron has developed efficient heterogeneous catalysts that eliminate ruthenium contamination in the final product.

## case study efficiency of exemplary ring-closing metathesis

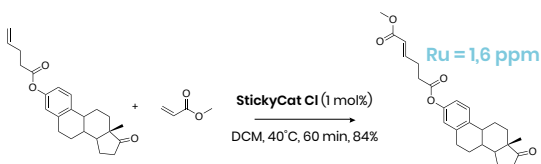


K. Skowerski, J. Pastva, S. J. Czarnocki, J. Janoscova; Exceptionally Stable and Efficient Solid Supported Hoveyda-Type Catalyst; Org. Process Res. Dev., 19 (7), 872-877, (2015)

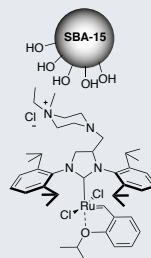
# Self-scavenging Catalyst

For homogeneous catalytic systems Apeiron designed self-scavenging metathesis catalysts assuring dual effect: excellent metathesis product yield and residual ruthenium levels below 5 ppm.

## case study efficiency in StickyCat Cl in cross metathesis



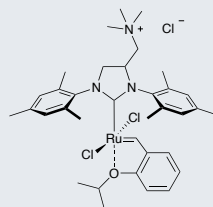
References: K. Skowerski, J. Pastva, S. J. Czarnocki, J. Janoscova; Exceptionally Stable and Efficient Solid Supported Hoveyda-Type Catalyst; Org. Process Res. Dev., 19 (7), 872-877, (2015)



## FixCat

AS2062 PCT/EP2013/053967

- Easy handling and removal (by simple filtration).
- No leaching - residual ruthenium < 10 ppm, often below 1 ppm.
- Excellent CM and RCM efficiency at very low catalyst loadings.
- Recyclable for up to 23 runs at 0.1 mol% catalyst loading.
- Compatible with multiple organic solvents.
- Applicable in continuous flow processes.



## StickyCat Cl

AS2041 PCT/EP2013/053967

- Simple removal by extraction with water or silica gel filtration.
- Residual ruthenium < 5 ppm.
- High activity at 40-110°C.
- Compatible with green solvents such as ethyl acetate and water.
- High stability in non-degassed water.
- Performance modulated by ion exchange.



## Contact:

### North America:

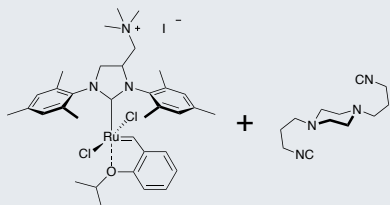
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## Self-scavenging metathesis catalyst working synergistically with metal scavengers

Apeiron has optimized its catalysts to function in concert with our metal scavengers to dramatically lower residual ruthenium levels. This approach is particularly well-suited for use where polar products with high ruthenium affinity present a complicated purification challenge, as is often observed in API production.

## StickyCat I

AS2047 PCT/EP2013/053967

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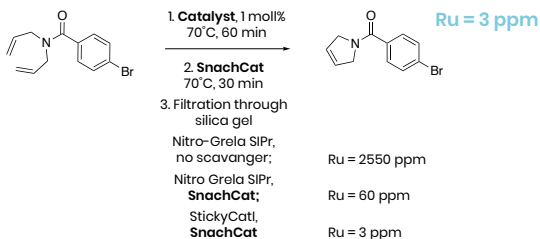
## SnatchCat

AS1033 PCT/EP2014/406739

- High efficiency: Ru < 10 ppm.
- Fast acting: 30 min scavenging time.
- Immediate reaction quencher.
- Simple workup: flash silica gel filtration.
- Compatible with broad range of functional groups and solvents.
- Facile handling - stable, non-toxic, non-volatile, odor-free.

## case study

reduction of ruthenium content after ring closing metathesis



### Typical procedure for metal scavenging

Add 4.4 eq of **SnatchCat** to a crude mixture containing metal ions or a catalyst (most effective solvents: toluene, dichloromethane, ethyl acetate). Stir for 30 minutes at room temperature. Filter through a silica pad (200 mg of silica gel 60 (230-400 mesh) per 1 mg of metals/catalyst). Note: scavenger equivalents, temperature as well as amount of silica gel for reactions of interest can be individually optimized.

References: G. Szczeplaniak, K. Urbaniak, C. Wierzbicka, K. Kosiński, K. Skowerski, K. Grela; High performance isocyanide scavengers use in low wastepurification of olefin metathesis products; ChemSusChem 8, 4139-4148, (2015)