



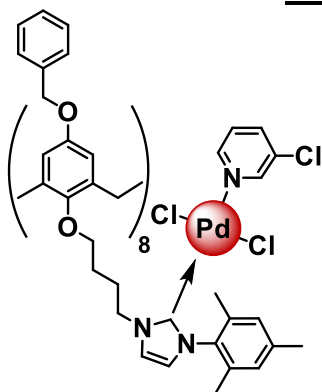
Supported catalysts for fine chemistry

NOVECAL is a French startup specialized in the design and synthesis of cyclic oligomers, and of related supported catalysts. Our palladium-NHC catalysts show excellent efficiency in Suzuki C-C and Buchwald-Hartwig C-N cross coupling reactions along with a low metal leaching inside products after filtration. We are currently developing rhodium-phosphine supported catalysts for hydrogenation, and cobalt-salen supported complexes for the opening of epoxides.

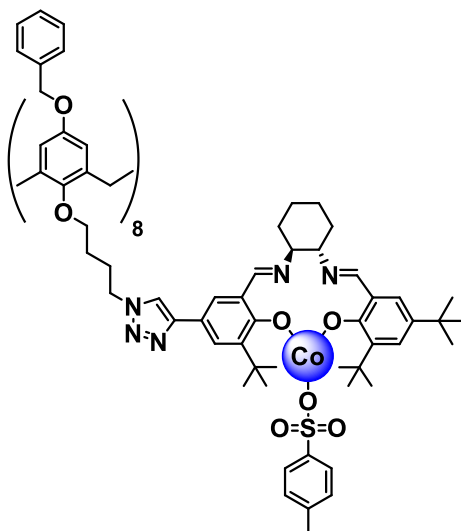
We also offer our expertise in various fields of catalysis:

- Cost optimization (catalysts screening and loading optimization, study and optimization of process parameters...)
- Custom catalysts heterogenization
- Realization and optimization of challenging reactions

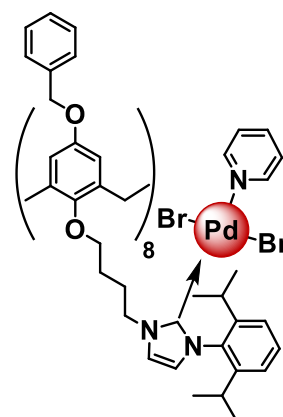
Structure of NOVECAL catalysts



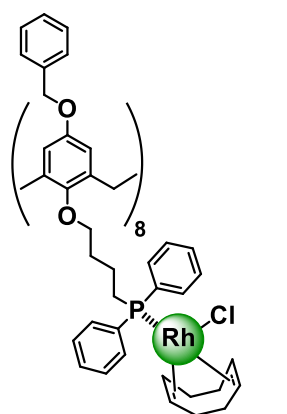
NOVECAT G1-01
Suzuki coupling



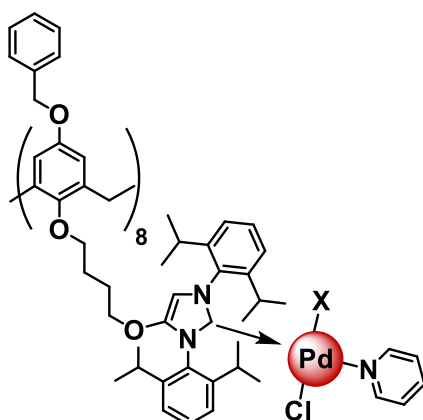
NOVECAT G1-04
Asymmetric epoxide opening



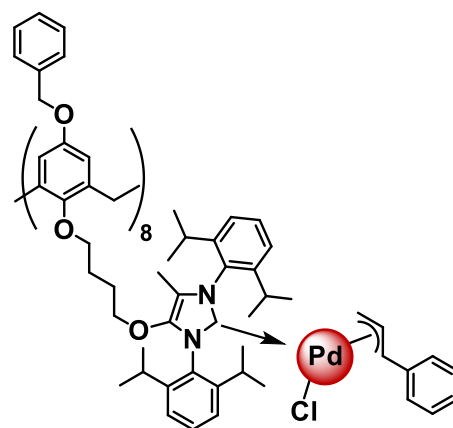
NOVECAT G1-02
Suzuki coupling with hindered substrates



NOVECAT G1-03
Hydrogenation reaction



NOVECAT G2
Suzuki coupling with challenging aryl halides

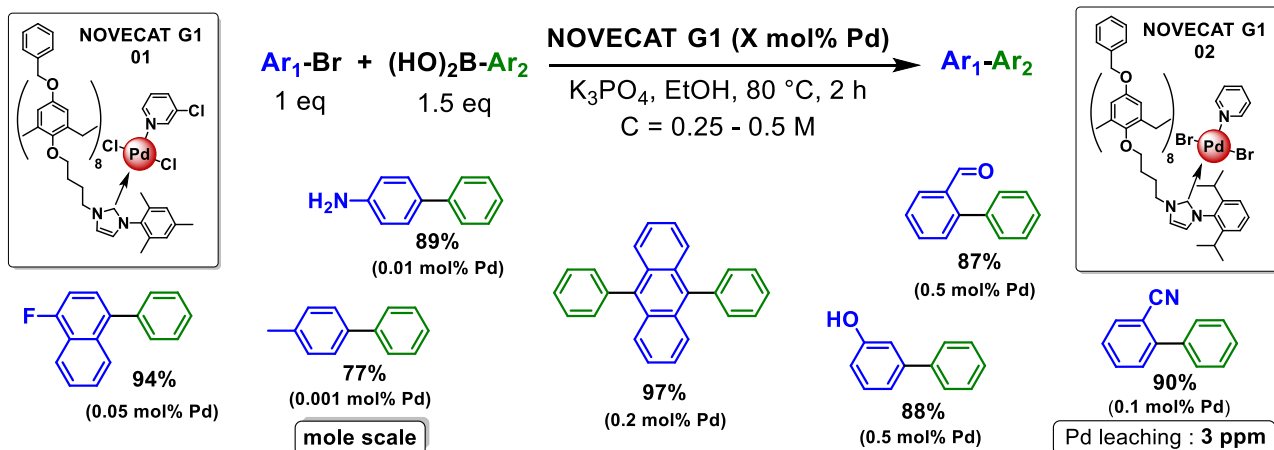


NOVECAT G3
Buchwald coupling with challenging substrates

General properties of NOVECAL catalysts

- Efficient at low catalytic loading
- Low metal leaching after simple filtration
- Robust structure, including high and reproducible metal content
- Air stable and easy to handle
- Compatible with diluted or concentrated reaction mixtures
- Soluble in polar solvents >> easy washing of the process equipment

Suzuki cross-coupling reaction with NOVECAT G1

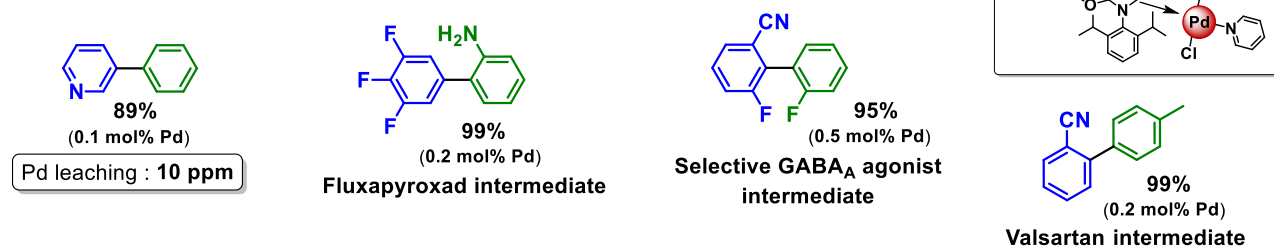


For publications on those results, see: a) *Dalton Trans.* **2018**, 47, 13843; b) *React. Chem. Eng.* **2020**, 5, 1509.

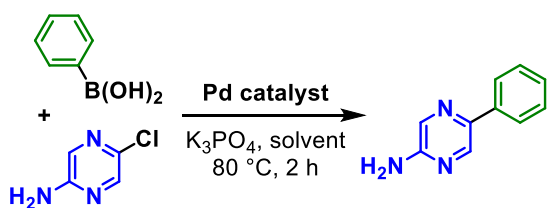
Suzuki cross-coupling reaction with NOVECAT G2



Preparation of pharmaceutical key intermediates from aryl bromides:



Comparison of Pd catalysts with functionalized aryl chlorides:



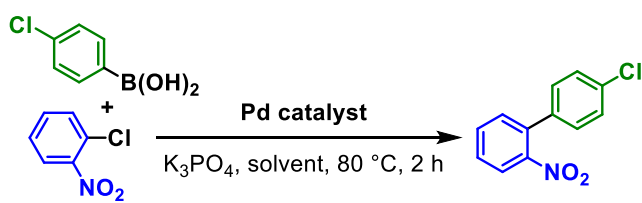
1 mol% **NOVECAT G2** : **94%**

1 mol% **Pd(OAc)₂/XPhos** : **87%**

1 mol% **Pd/C** : **0%**

1 mol% **Pd(PPh₃)₄** : **4%**

Intermediate of a highly selective drug candidate for obesity treatment



0.5 mol% **NOVECAT G2** : **88%** (Pd leaching : **31 ppm**)

0.5 mol% **Pd(OAc)₂/XPhos** : **88%** (Pd leaching : **1450 ppm**)

1 mol% **Pd/C** : **5%**

1 mol% **Pd(PPh₃)₄** : **29%**

1 mol% **PEPPSI-IPr** : **68%**

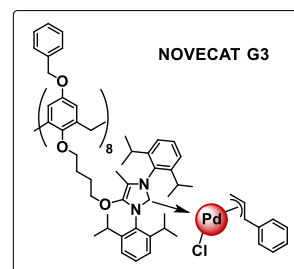
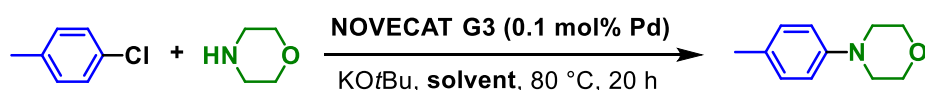
Boscalid intermediate

Advantages of NOVECAT catalysts for Suzuki C-C coupling:

- Efficient with a wide range of substrates
- Low catalytic amount required
- Low leaching levels after simple filtration
- Performant with both aryl chlorides and bromides

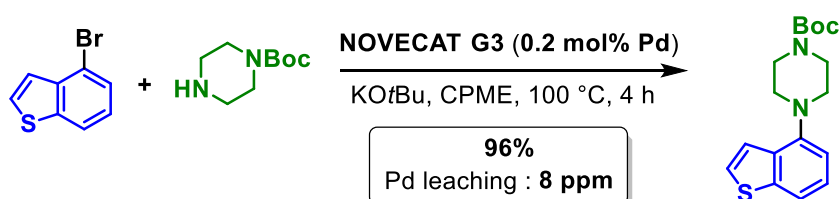
Buchwald-Hartwig C-N coupling

Screening of solvents with an aliphatic amine:

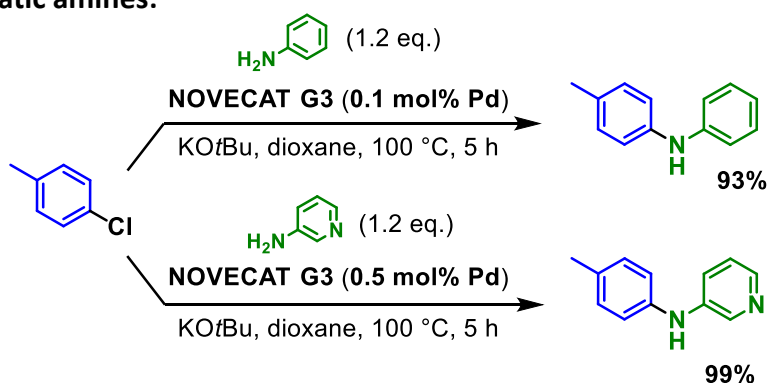


Solvent	Yield (%)	Pd content after filtration (ppm)
MeTHF	99	24.5
Dioxane	99	25
CPME	93	38
Toluene	82	-
Methylcyclohexane* (1 mol% Pd)	95	30

Application for the preparation of Brexpiprazole's key intermediate:



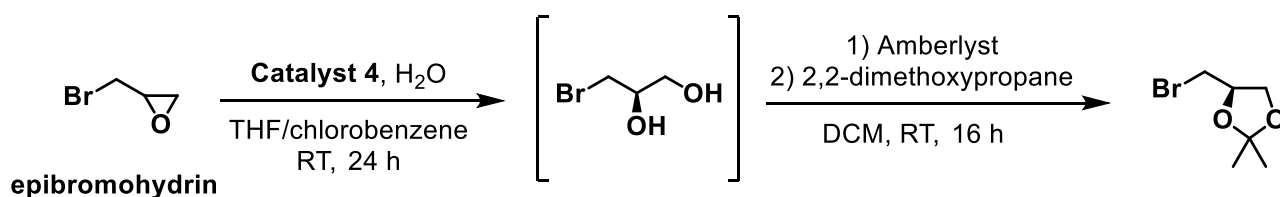
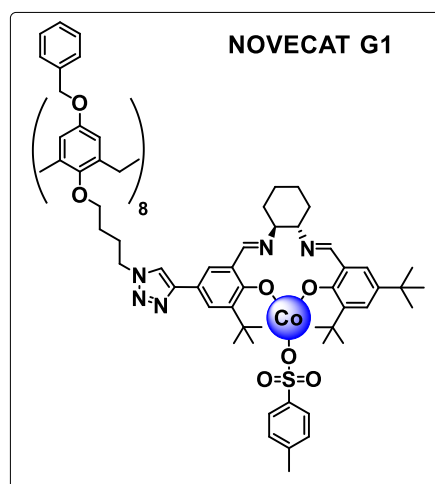
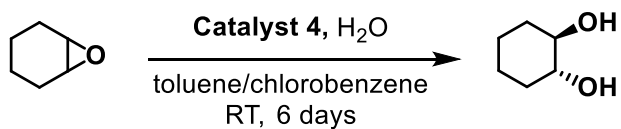
Coupling with aromatic amines:



Advantages of NOVECAT catalysts for Buchwald C-N coupling:

- Low catalytic loadings
- Low leaching after simple filtration
- Compatible with various attractive solvents for industry
- Procedure applicable to both aryl chlorides and bromides
- Efficient with chelating amines
- Easy washing of the equipment at the end of the reaction

Asymmetric epoxide ring-opening

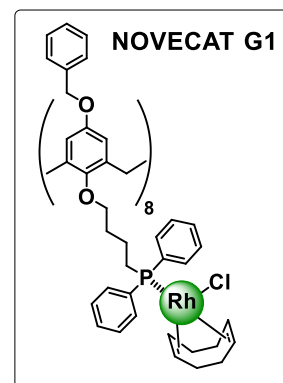
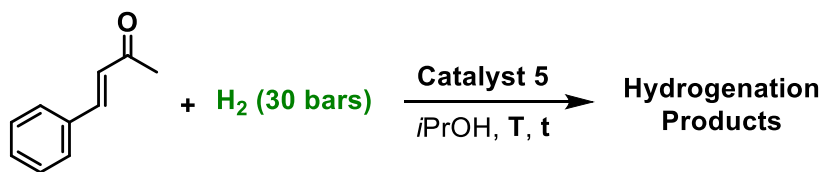


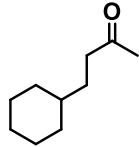
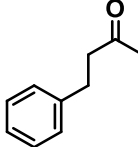
Product	Co (mol%)	Conversion (%)	e.e. (%)	[Co] _{Product} (ppm)	Co eliminated (%)
	2	100	76	-	-
	1	100	94	0.7	99.98

Recycling experiments performed on asymmetric epibromohydrin ring-opening:

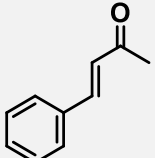
Product	Cycles	Co (mol%)	Conversion (%)	e.e. (%)
	Cycle 1	2	100	94
	Cycle 2	2	100	94

Hydrogenation reaction



Rh (mol%)	T (°C)	t (h)	Conversion (%)		
0.05	100	2	100	> 95%	
0.3	25	72	100		> 92%

Residual metal content inside products after filtration (leaching)

Substrate	Rh (mol%)	T (°C)	t (h)	Conversion (%)	Residual metal content (ppm)
	0.05	100	3	100	2.4
	0.3	25	49	98	6.2