Polyurea Microencapsulated Palladium Catalysts

Pd EnCat™

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Outline

- Introduction
- Catalyst synthesis
- Catalyst physical characteristics
- Catalyst activity optimisation
- Catalyst mechanism
- Chemistry examples
- Parallel synthesis examples
- Process Case Studies

Introduction

Pd Catalysed Reactions: A Pivotal Tool in the Chemists 'Tool Box'

- Pd catalysed C-C bond formations
  - Heck, Suzuki, Stille, Carbonylation, Sonogashiras, etc
- Pd-Catalysed C-O,C-N,C-S bond formation.
- Pd reductions/oxidations

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Common Process Issues with Homogeneous Pd Catalysis

- Pd contamination of product – regulatory requirements
- Pd contamination of intermediate – interferes with downstream chemistry
- Pd contamination of reactor vessels – cleaning costs
- Pd contamination in waste streams – treatment costs
- Pd loss from process = high cost

Catalyst Synthesis

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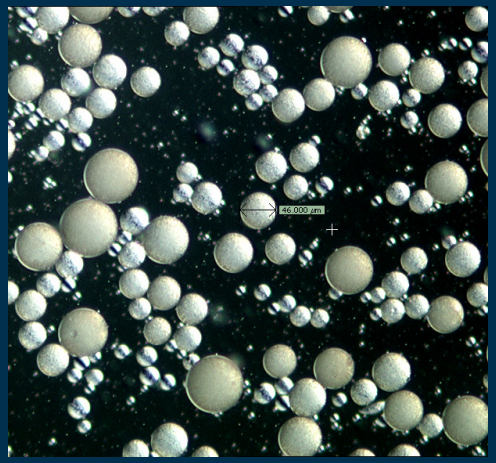
Microencapsulation of Palladium (II) Salts by *in situ* Interfacial Polymerisation

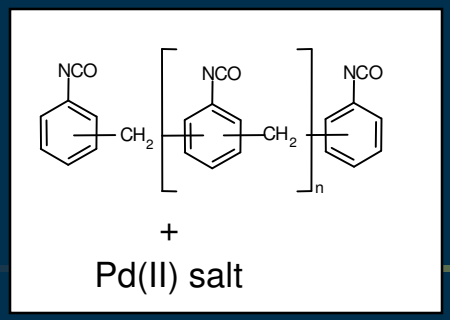


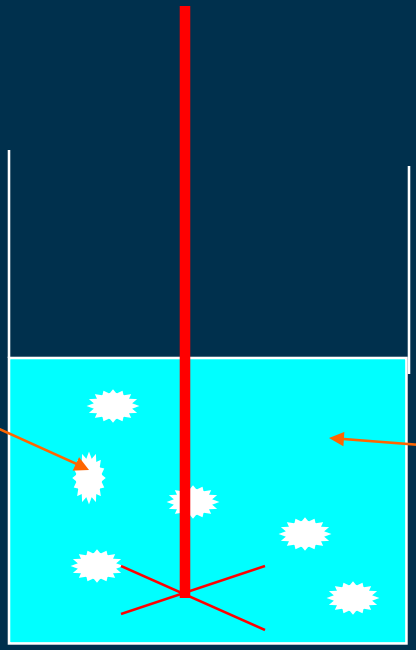
Oil-in-water emulsion

Heating initiates polymerisation

Filtered & dried EnCat™ 50-300µm

Catalyst in organic solvent with cross-linking isocyanates





water, stabilisers

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Catalyst Physical Characteristics

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SEM 0.4 mmol/g Pd EnCat™ 40

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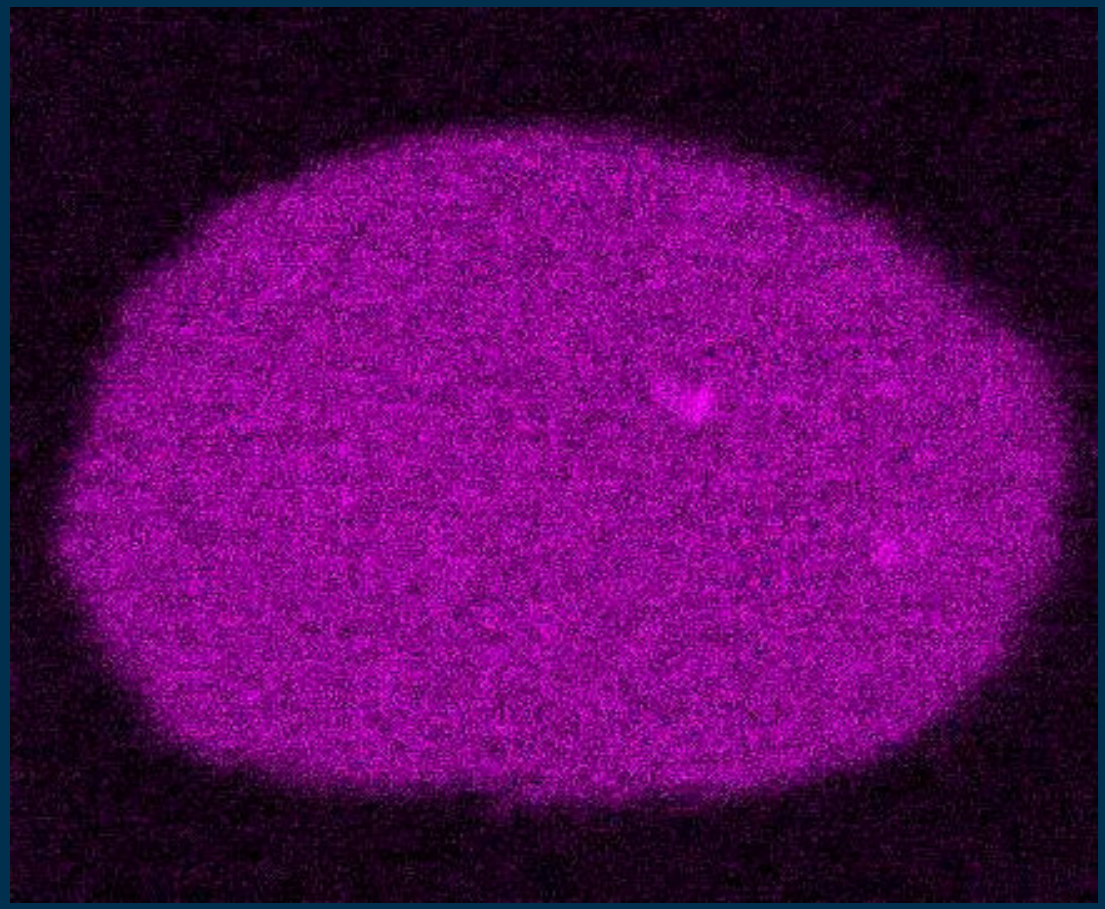
EDX Analysis 0.4 mmol/g Pd EnCat™ 40



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Dry State Porosity of 0.4 mmol/g Pd EnCat™ 40

- BET nitrogen adsorption surface area = 0.07m^2/g

  - no meso or macro pores

- Mercury intrusion porosimetry = 0.06cc/g

  - no macro pores
  - some partial collapse of internal voids

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Solvent Swelling Of Pd EnCat™ 40

Solvent	Swelling of EnCat™ %
DMF	110
DMA	**100**
THF	10
Acetone	**20**
EtOH	10
IPA	**5**
Toluene	0

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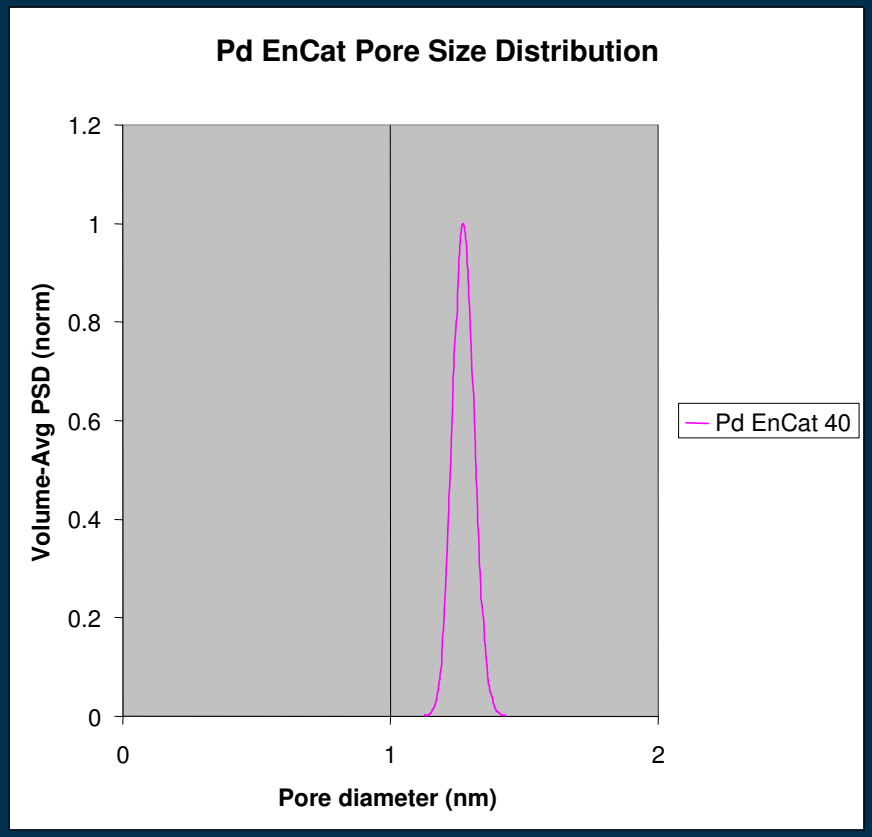
Porosity of 0.4 mmol/g Pd EnCat™ 40 In THF swollen state

Chromatographic Porosimetry investigation:



- Low pore size - average pore diameter = 1.28nm
- Very low pore volume
- Mono dispersed pores
- Polystyrene molecules of MW >300 are excluded

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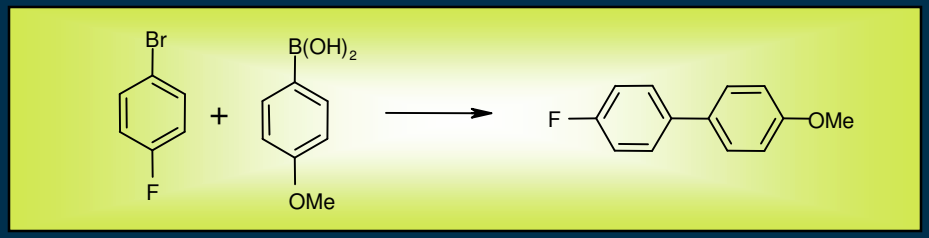
Leaching of Pd from Pd EnCat™ 40

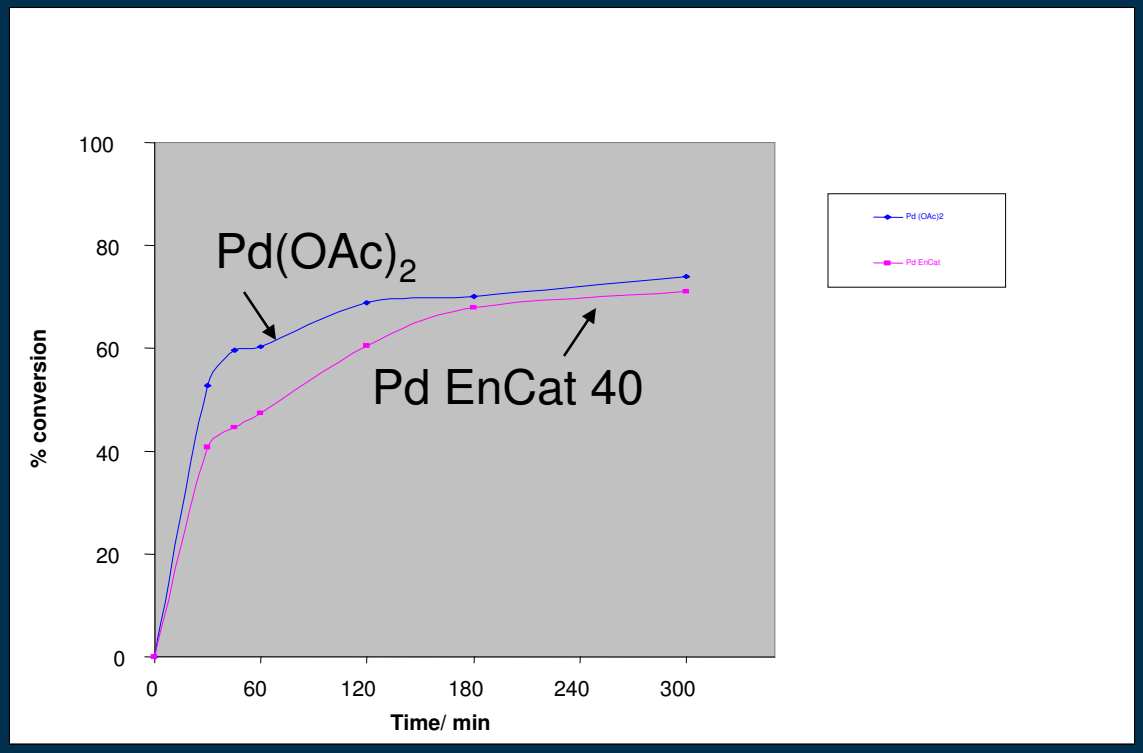
Solvent	Pd ppm	% Pd extracted
THF	1	0.15
Acetone	<1	<0.15
Ethanol	<1	<0.15
Acetonitrile	1	0.15
IPA	<1	<0.15
Toluene	<1	<0.15
Dioxane	1	0.15
Ethyl acetate	<1	<0.15
DMF	7	1.08
DMA	6	0.93

Pd EnCat™ 40 Comparison with $Pd(OAc)_2$ in Simple Suzuki Coupling



Conditions: 3 mol% Pd, K_2CO_3, 80°C, EtOH/Water 20/1

Reaction stopped after 5 hours



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Pd EnCat™ Activity Optimisation

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Enhancement of Pd EnCat™ Activity

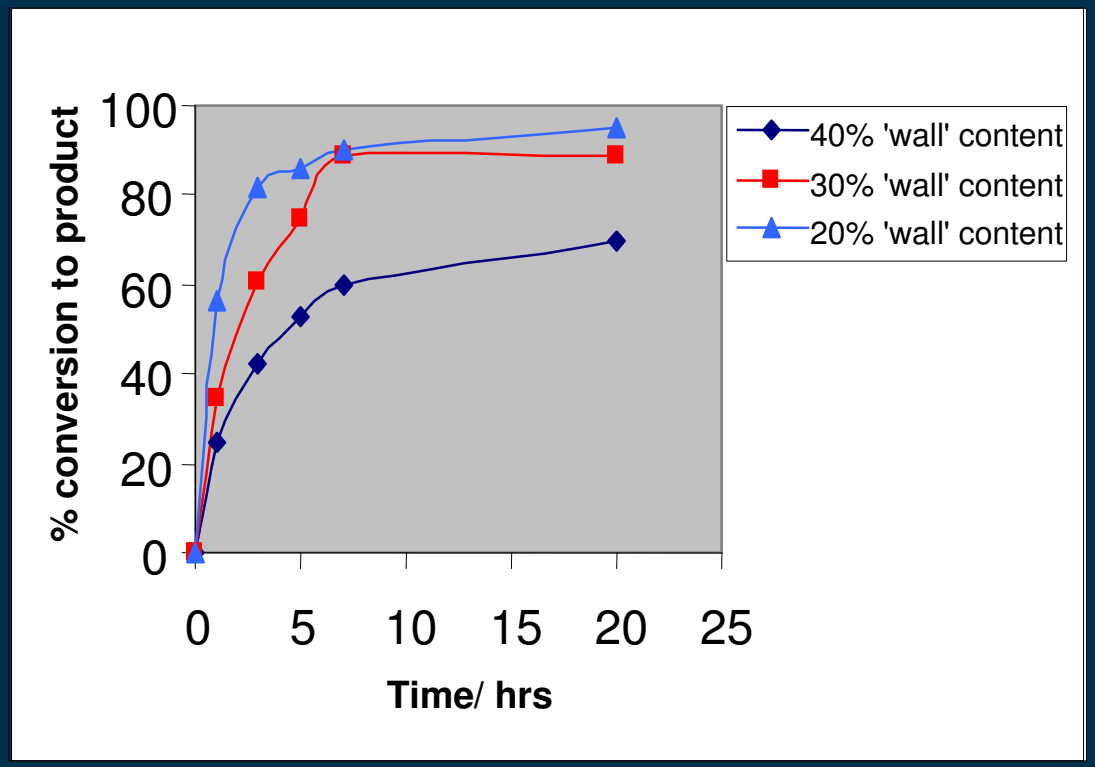
Achieved through increasing matrix porosity - improving access of substrates to metal species

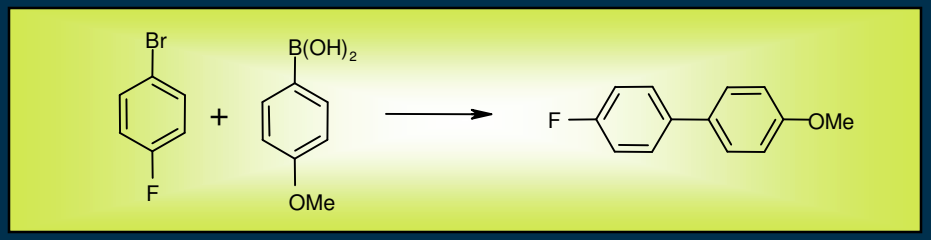
1) Reducing polymer matrix content

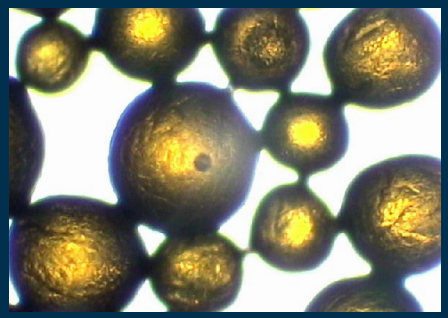
2) Reducing cross-link density of PU matrix

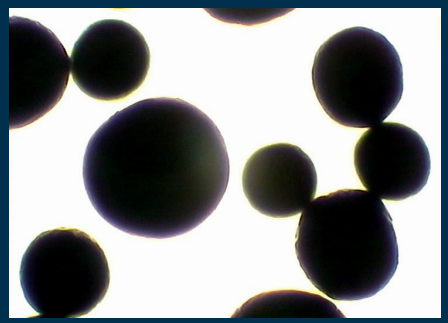
3) Use of solvents capable of swelling matrix

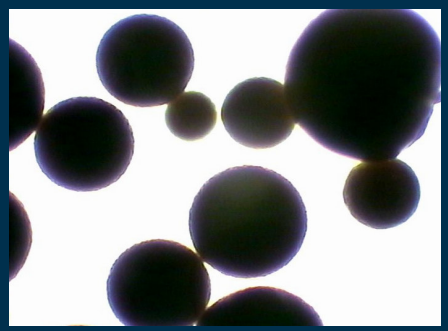
Reducing Polymer Matrix Content











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Porosity in Solvent Swollen State as a function of Matrix Content

Chromatographic Porosimetry Investigation:

Matrix Content (%)	20	30	40
Swollen Bulk density (g/ml)	0.25	0.33	0.707
Swollen Pore volume (ml/g)	2.8	1.5	0.3
Average Pore Diameter (nm)	1.3	**2.4**	1.4
PS MW Exclusion	>300	**>900**	>300

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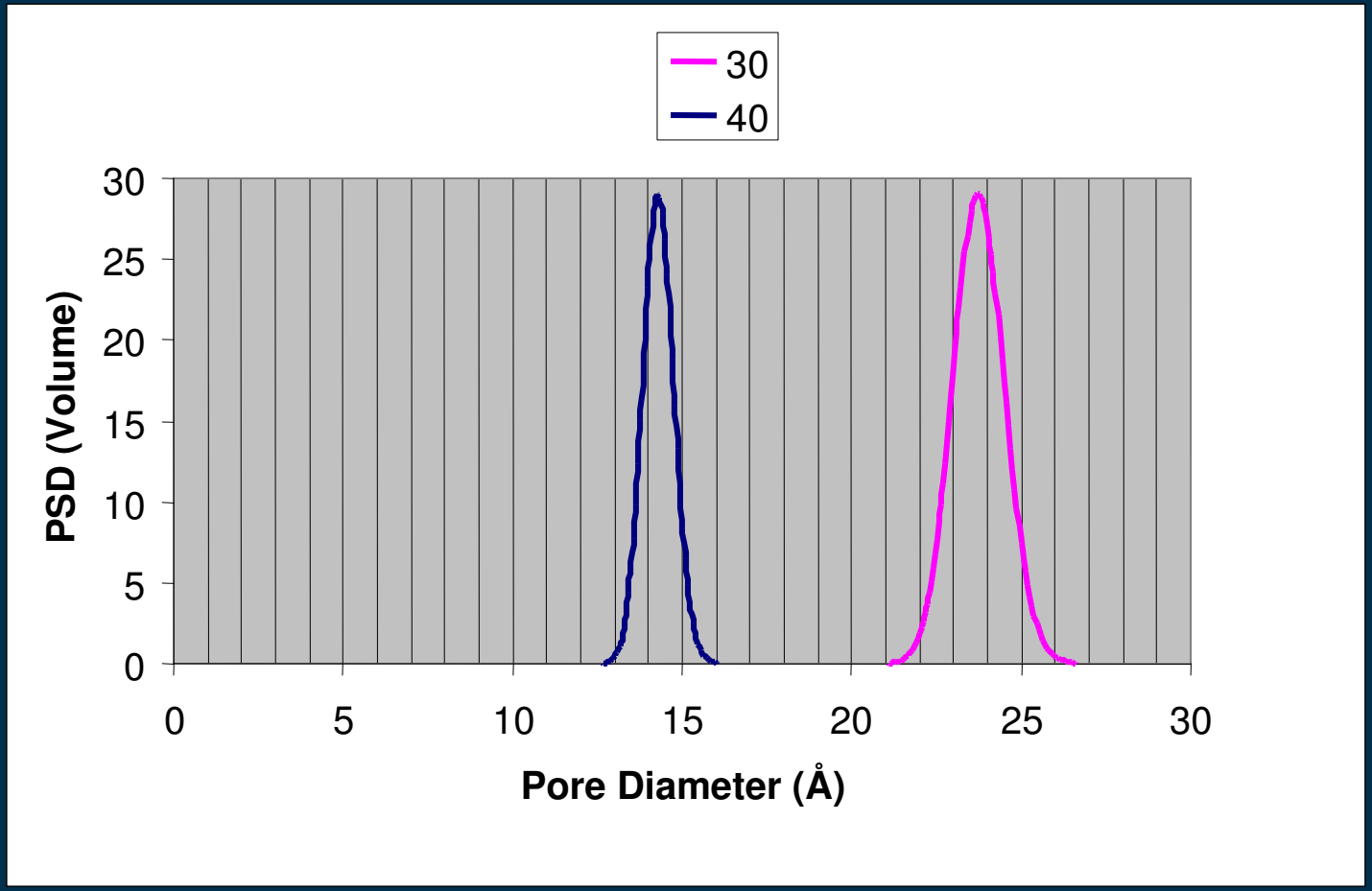
Pore Size Distribution in Solvent Swollen State



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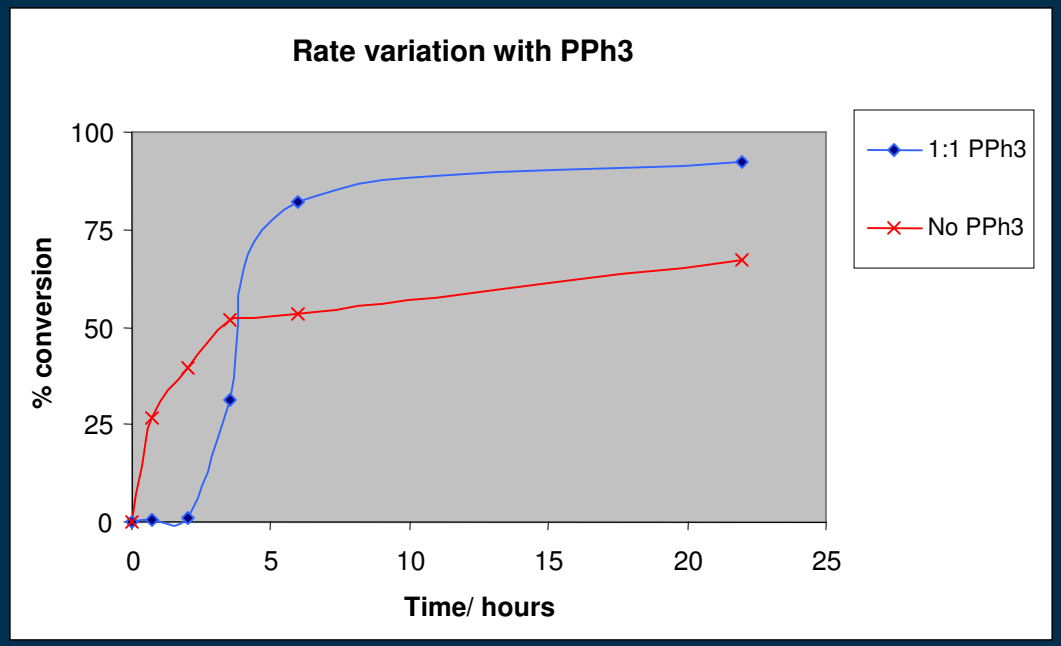
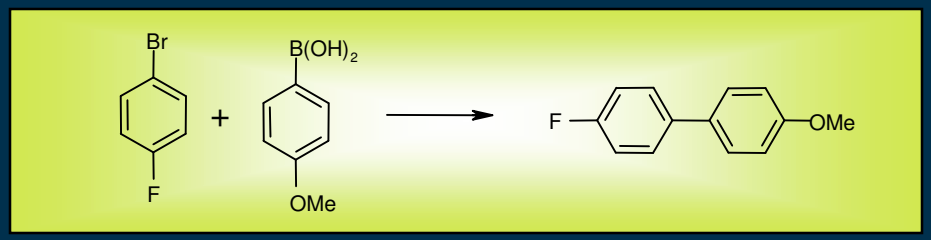
Leaching of Pd from Pd EnCat™ 30

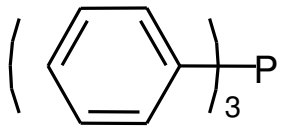
Solvent	Pd ppm	% Pd extracted
THF	4	0.31
Acetone	1	0.08
Ethanol	<1	<0.08
Acetonitrile	<1	<0.08
IPA	<1	<0.08
Toluene	<1	<0.08
Dioxane	<1	<0.08
Ethyl acetate	<1	<0.08
DMF	5	0.39
DMA	3	1.01

Post Addition Of TPP to Pd EnCat™ 40 Suzuki Coupling Reaction



- Initial induction period before reaction starts
- Low levels (<3 ppm) Pd detected in solution



TPP = 

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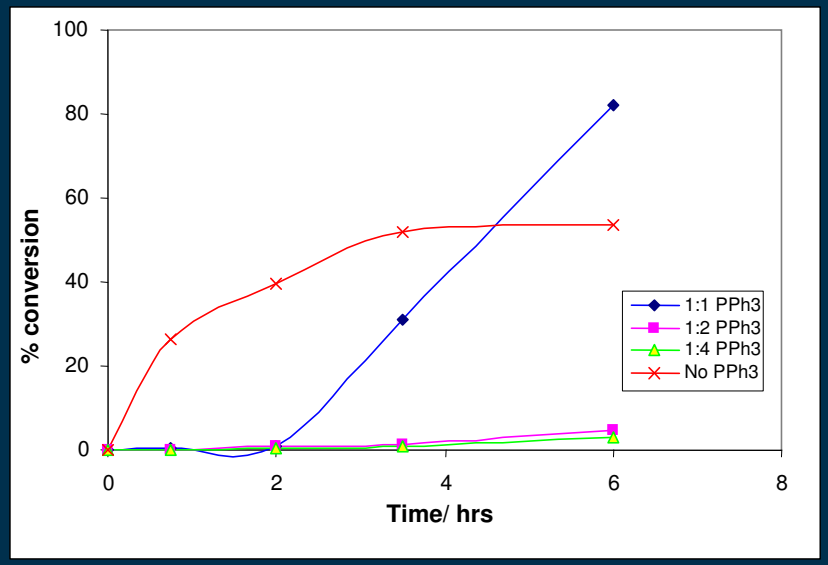
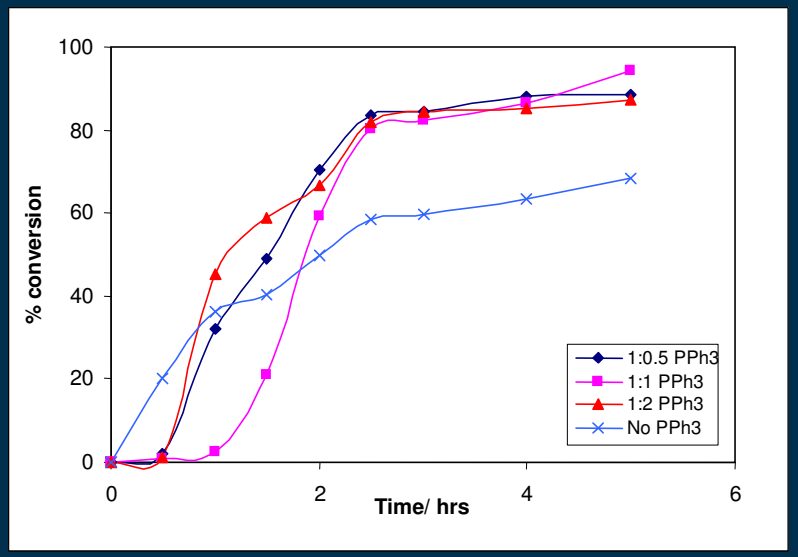
Initial Kinetics Following Post Addition Of TPP to Pd EnCat™ 40 and 30

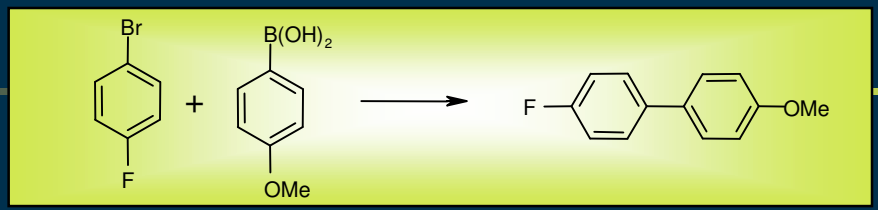
Pd EnCat™ 40



Pd EnCat™ 30



- Pd EnCat™ 30 shorter induction
- Induction period is sensitive to the amount of TPP



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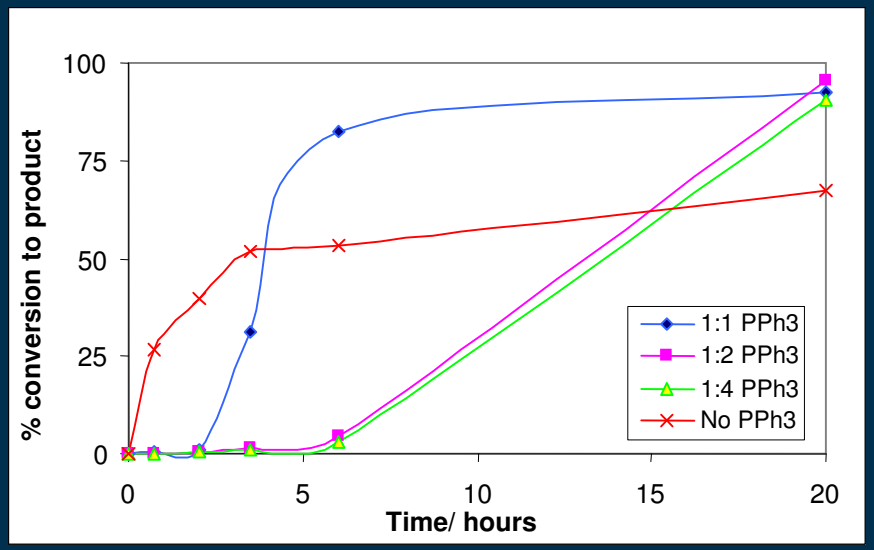
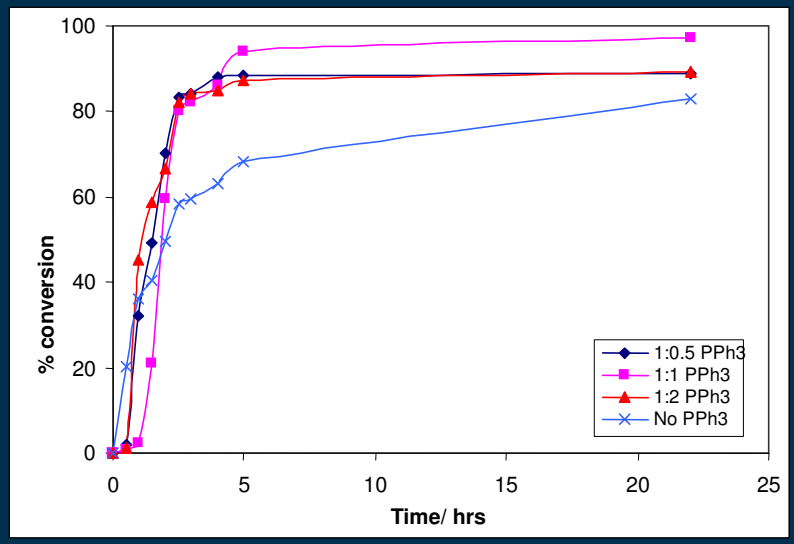
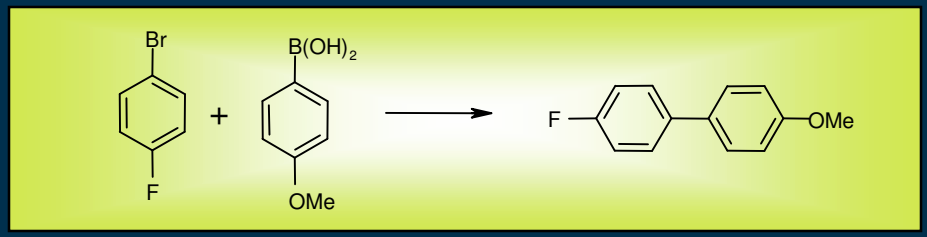
Overall Kinetics Post Addition Of TPP to Pd EnCat™ in Suzuki Coupling Reaction

Pd EnCat™ 40



Pd EnCat™ 30





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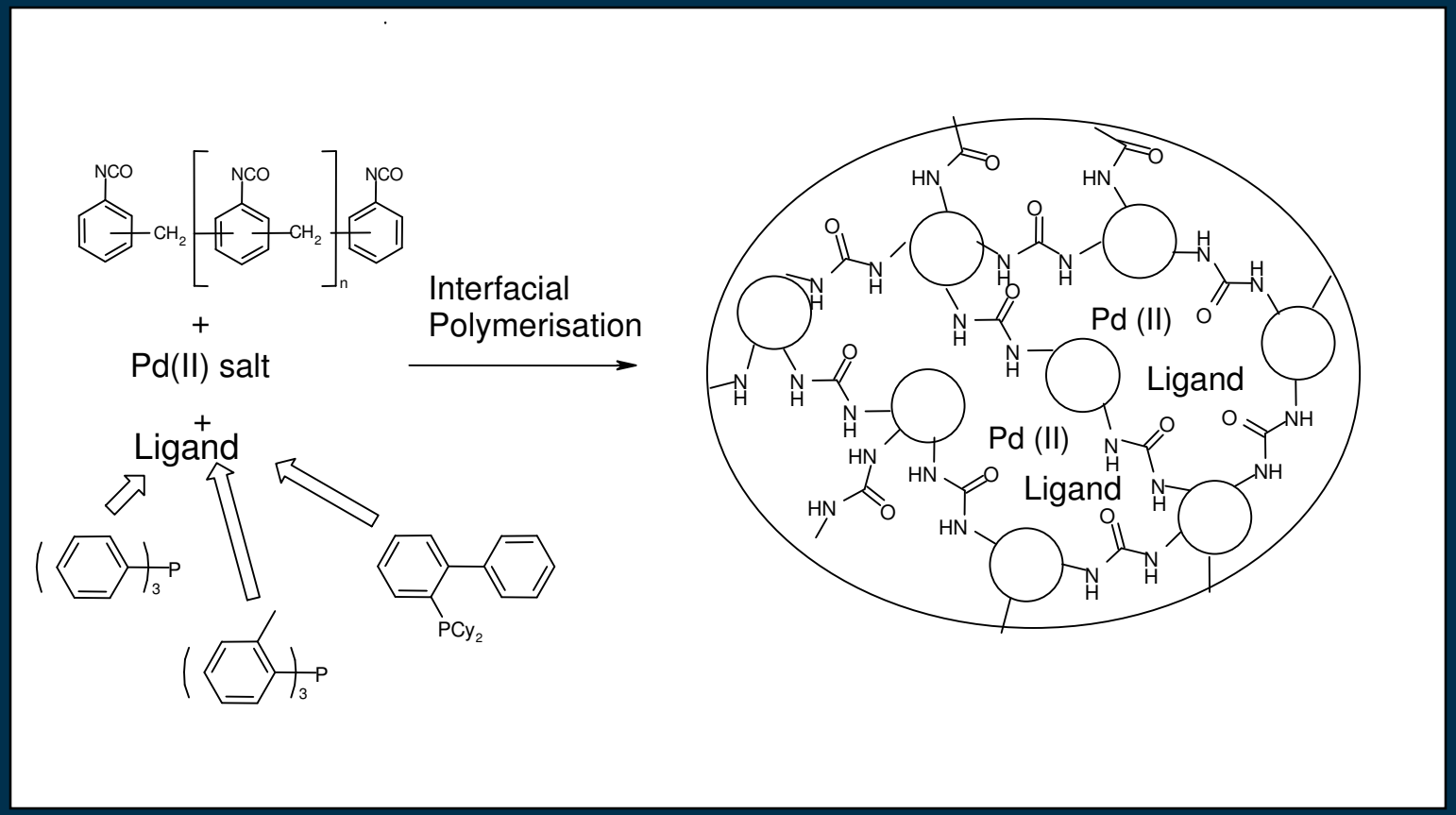
Pd EnCat™ with Co-Encapsulated Phosphine Ligand



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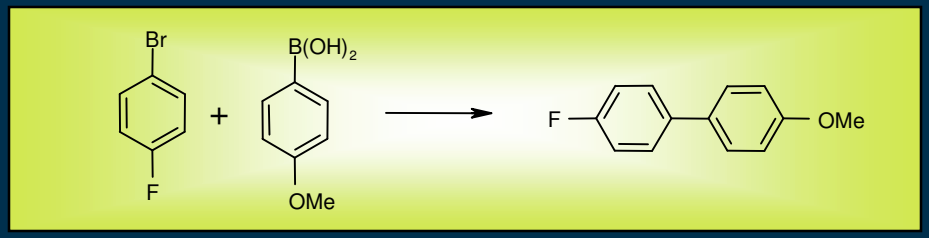
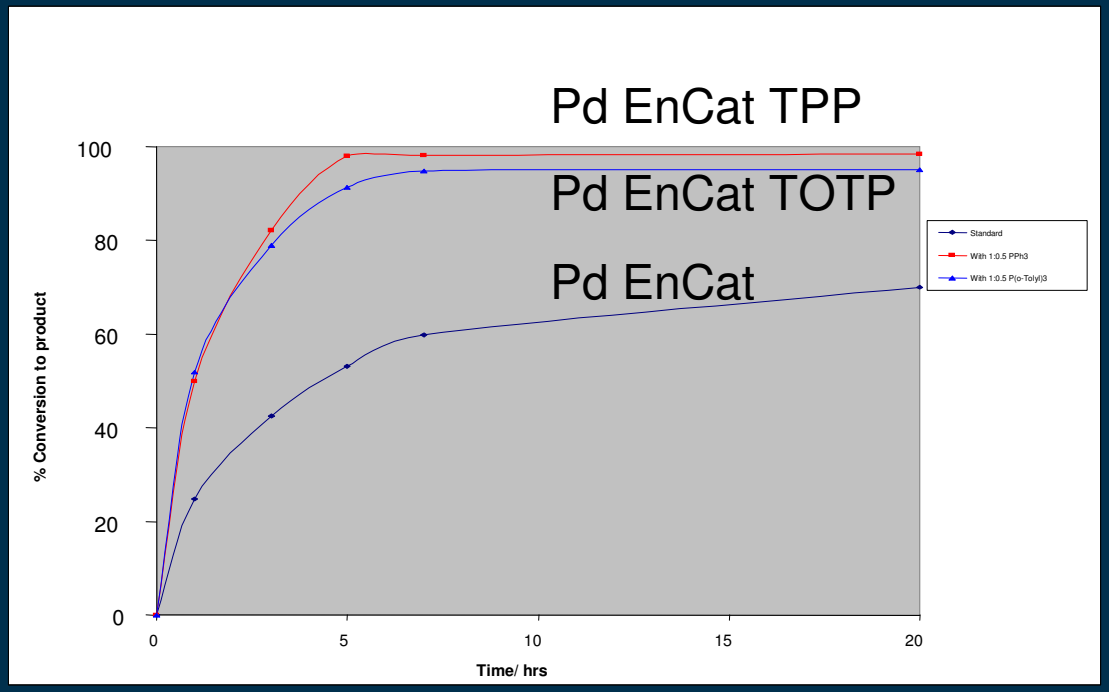
Pd EnCat™ Activity with Co-Encapsulated Phosphine Ligands (Pd/P 1/0.5)



Ar = Phenyl TPP

Ar = o-Tolyl TTP



Crude Product

<5ppm Pd
<5ppm P

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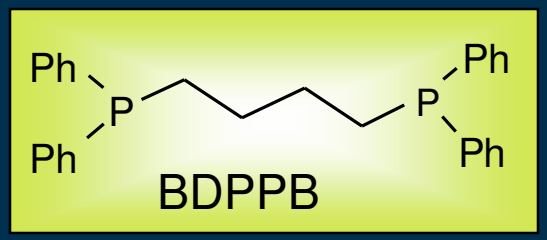
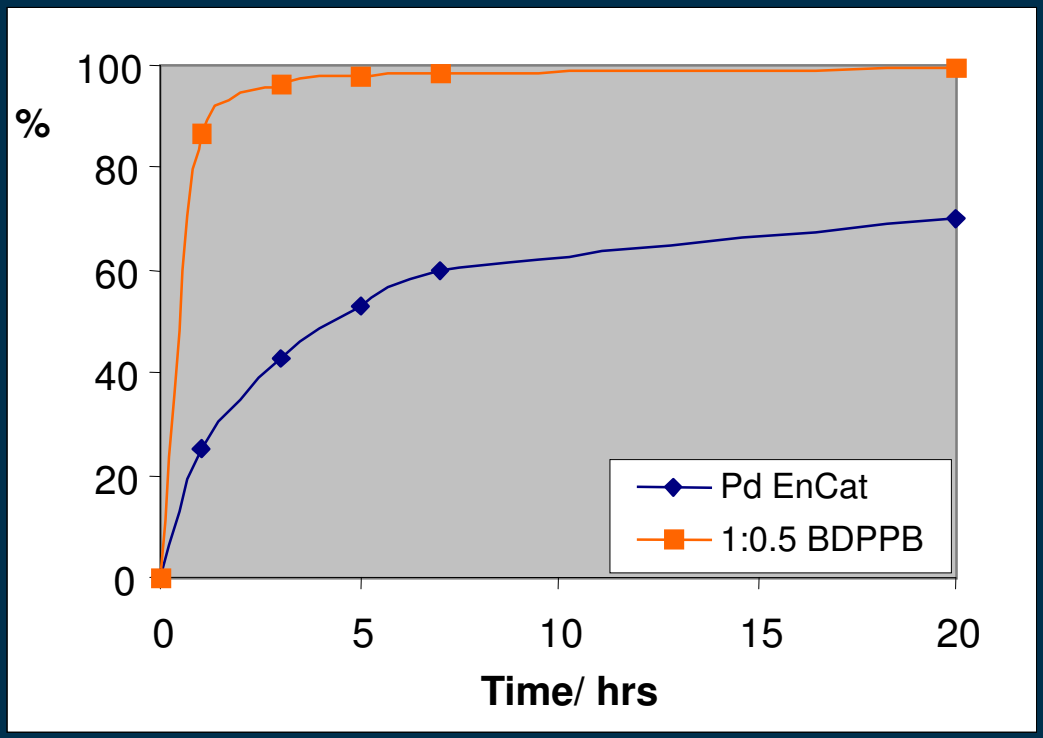
BDPPB Pd EnCat™ Activity



Conditions: 3 mol% Pd, K_2CO_3, 80°C, IPA/Water 20/1



Crude Product
20ppm Pd
50ppm P

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Pd EnCat™ with Co-encapsulated Phosphine Ligand

- Fast reactions in quantitative yield
- Low palladium leach (<15ppm, <1% total)*
- Some phosphine ligand leach (<30ppm, <10% total)*
- Greatly simplified reaction work up
- Versatile ‘tunable’ catalyst design

* Solvent dependent

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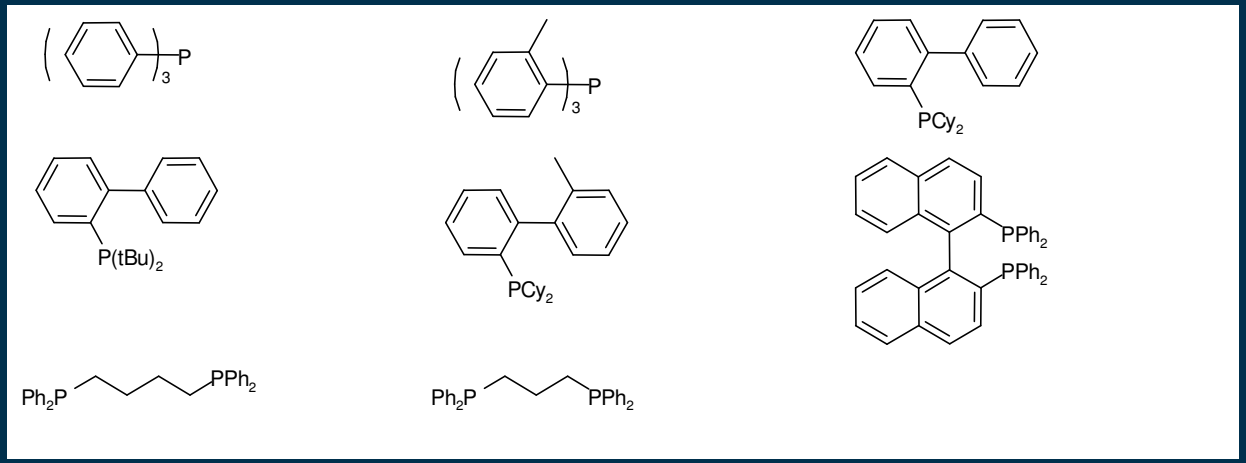
Customised Catalysts

Pd EnCat™ catalysts - can be tailored to a specific process and chemistry by selection of:

- Metal type and loading
- Ligand type and loading
- Matrix porosity and particle size



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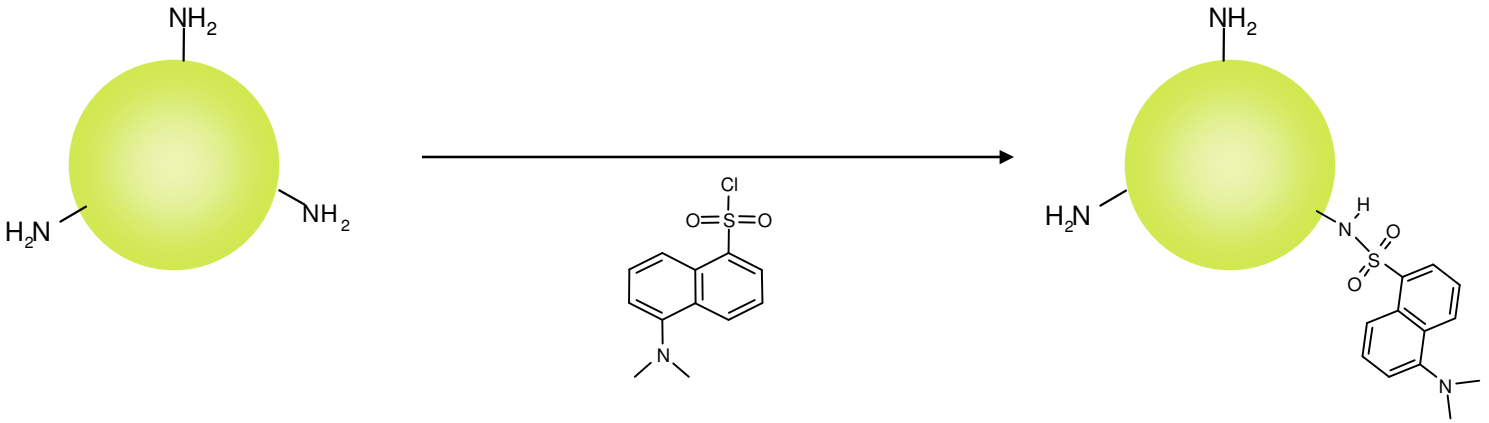
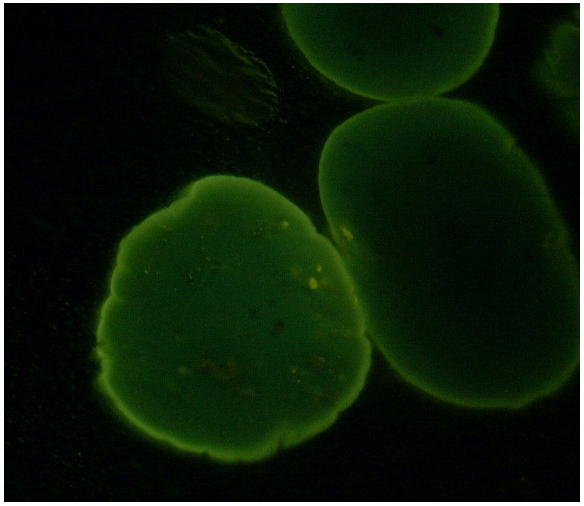
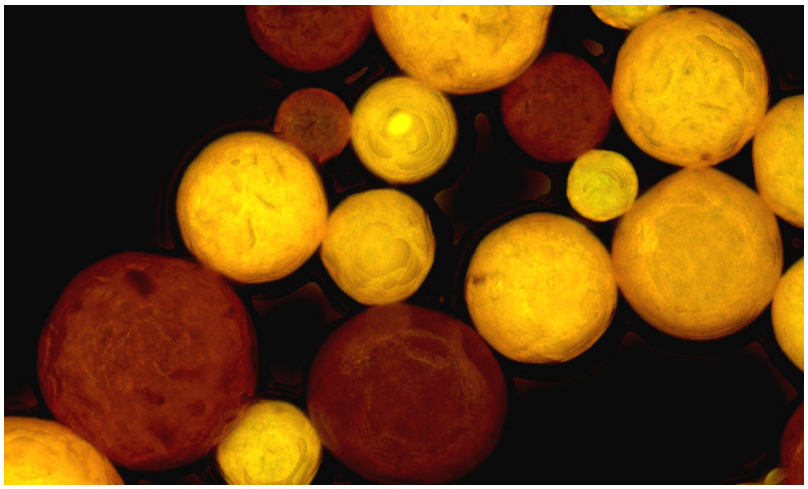
Fluorescent Labelled Pd EnCat™







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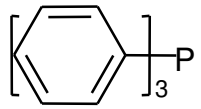
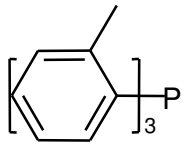
Microencapsulated Palladium Acetate Products

Product	Matrix Content %	Pd content mmol/g (%)	Co-encapsulated ligand	Average particle size micron
Pd(II) EnCat™ 40	40	0.4 (4)	-	150-200
Pd(II) EnCat™ 30	30	0.4 (4)	-	150-200
Pd(II) EnCat™ TPP30	30	0.4 (4)		150-200
Pd(II) EnCat™ TOTP30	30	0.4 (4)		150-200

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Microencapsulated Palladium Zero Nano Particulate Products

Product	Matrix Content %	Pd content mmol/g (%)	Co-encapsulated ligand	Average particle size micron
Pd(0) EnCat™ 40NP	40	0.4 (4)	-	150-200
Pd(0) EnCat™ 30NP	30	0.4 (4)	-	150-200

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Pd EnCat™ Mechanism

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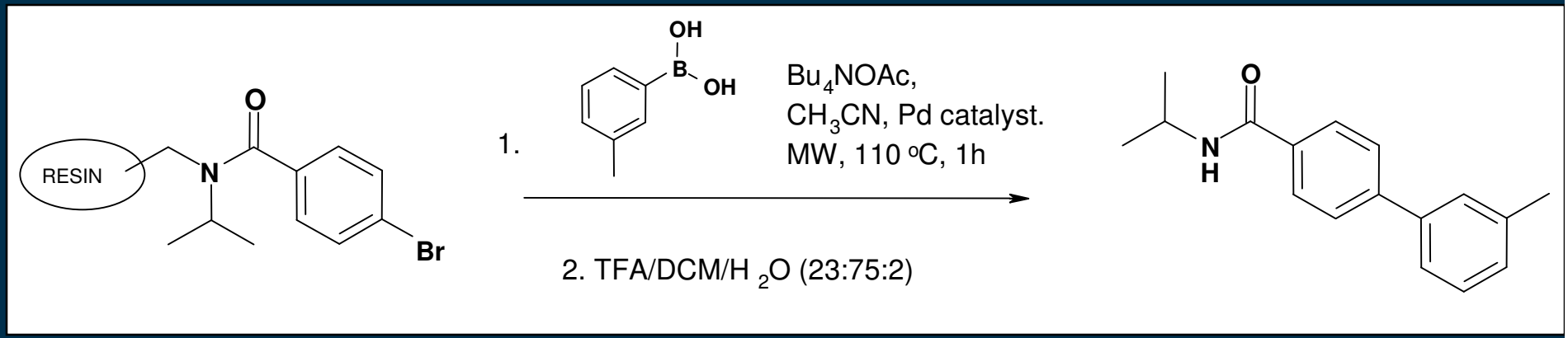
Catalyst Mechanism



- **Control reactions with $Pd(Ph_3)_4$ gave 4:1 product : Ar-Br**
- **Pd-EnCat™ - no detectable product. Only pure Ar-Br**

c.f. I. W. Davies *et. al., J. Am. Chem. Soc.*, **2001**, *123*, 10139-10140

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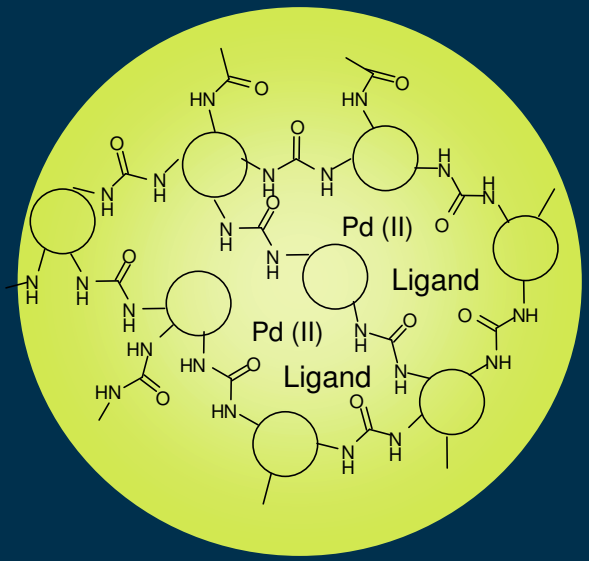
Catalyst Mechanism

Reaction probably takes place within microcapsules:

- Suzuki substrates added to hot solvent extracts of Pd EnCat™ gave no reaction.
- Removal of Pd EnCat™ from Suzuki reaction mixture by hot filtration stopped reaction.

Mechanism

REAGENTS



PRODUCTS

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Chemistry Examples with Pd EnCat™

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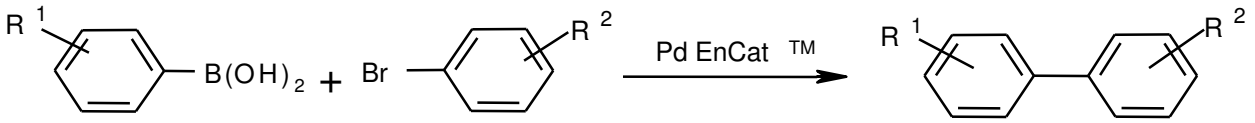
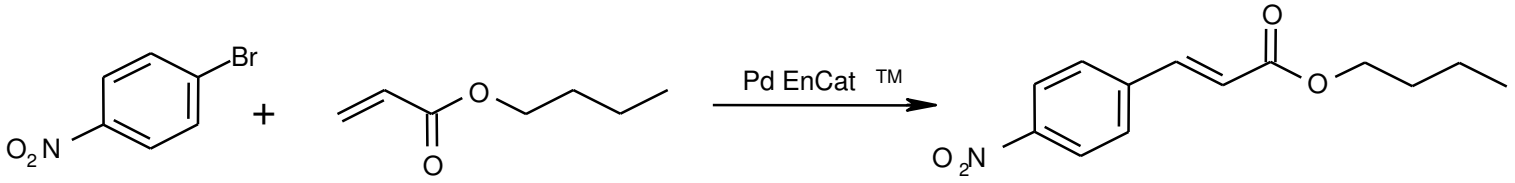
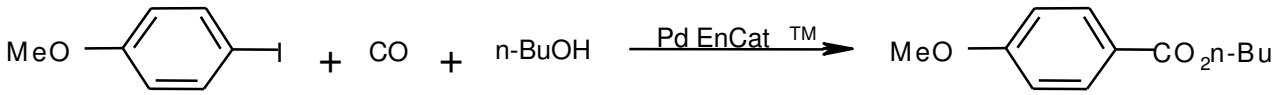
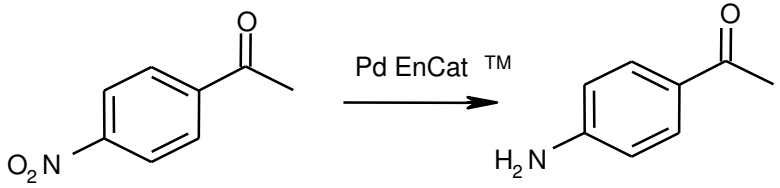
Chemistry Examples

Suzuki:	
Heck:	
Carbonylation	
Transfer Hydrogenation	

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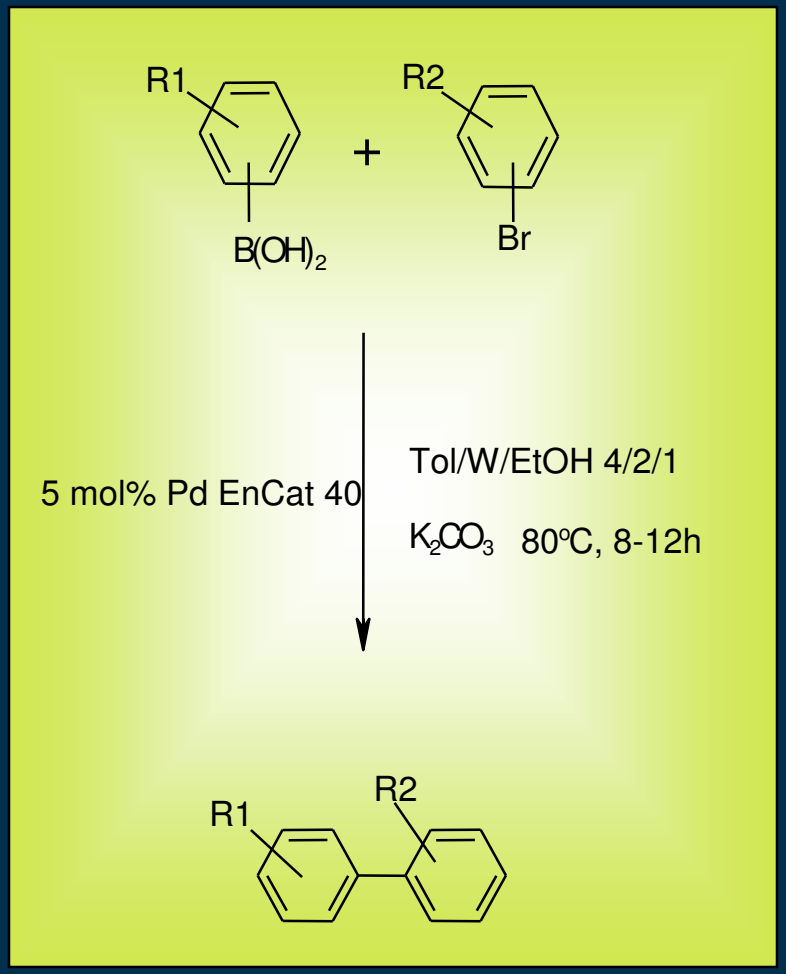
Suzuki Couplings Catalysed by Pd EnCat™ 40



R1	R2	Yield %
p-OMe	p-OMe	87
p-OMe	p-F	89
p-OMe	p-NO_2	91
o-OMe	o-OMe	71
p-Ac	p-OMe	84
p-Ac	p-F	90
p-Ac	p-NO_2	97
H	p-OMe	94
H	p-F	93
H	p-NO_2	97

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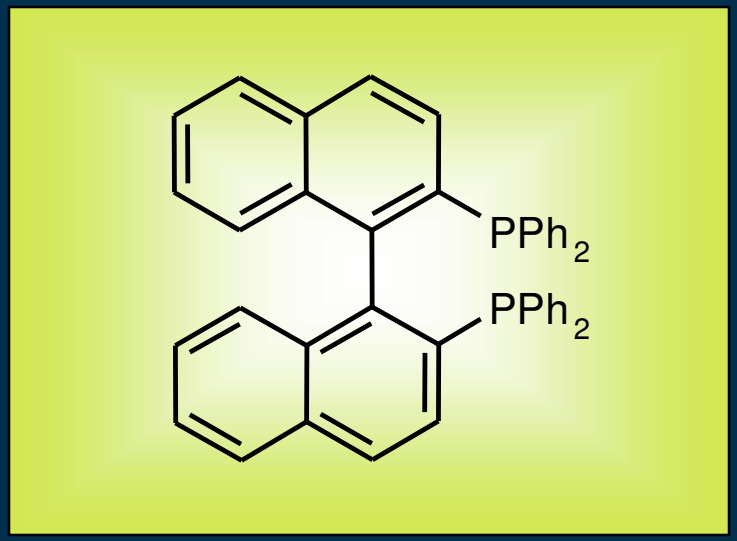
Pd EnCat™ Development Product

Pd EnCat™ Binap30



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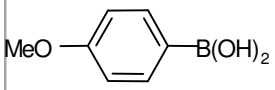
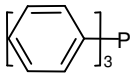
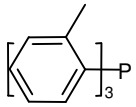
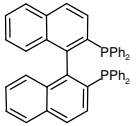
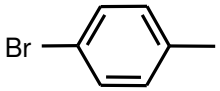
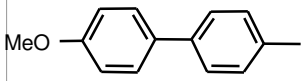
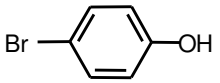
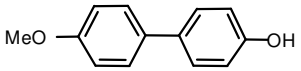
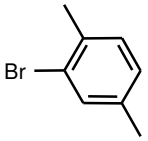
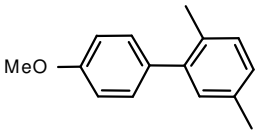
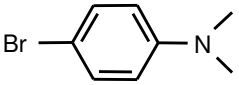
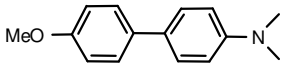
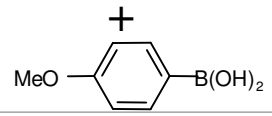
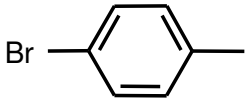
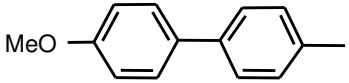
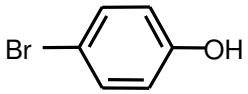
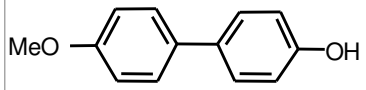
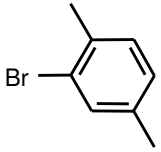
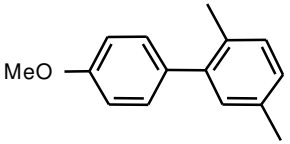
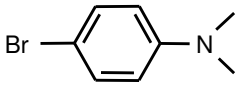
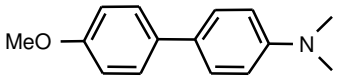
Electron Rich Suzuki Couplings
Pd EnCat™ Binap30 Catalysed

Aryl Halide + 	Product	Encap Ligand (% Yield)			
		None	TPP 	TOTP 	Binap 
		55	74	76	>99
		27	15	2	50
		53	76	91	>99
		68	61	100	97

Avecia

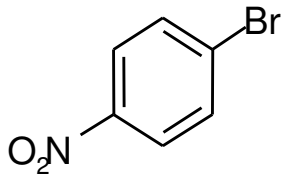
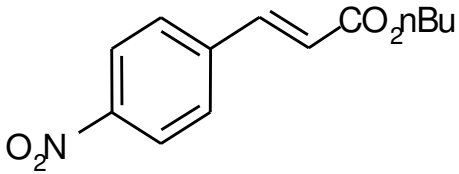
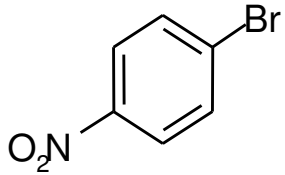
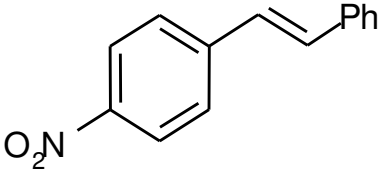
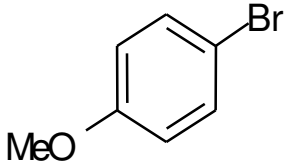
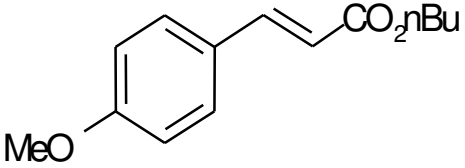
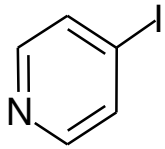
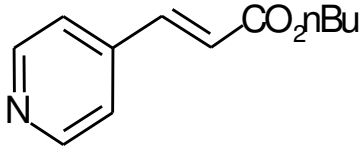
Pd EnCat™ Binap30 Catalysed Electron Rich Suzuki Couplings

Aryl Halide + 	Product	% conv	*Pd ppm	*P ppm
		>99	2	30
		50	3	38
		>99	2	34
		97	5	47

* In crude product following solvent evaporation

Avecia

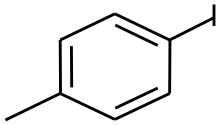
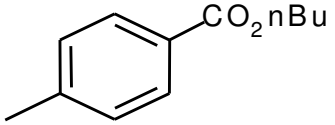
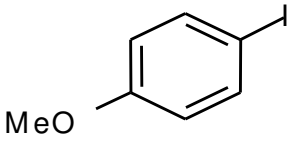
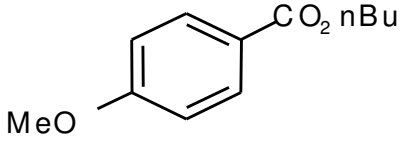
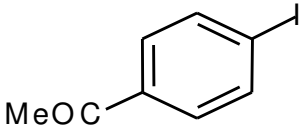
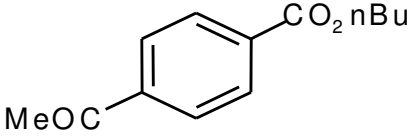
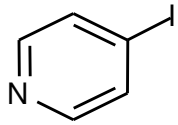
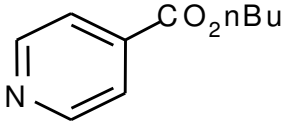
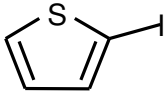
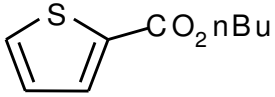
Pd EnCat™ 40 Catalysed Heck Reactions

Substrate	Product	Yield (%)
		91
		93
		25
		98

Conditions: 2.5mol% Pd EnCat™ 40, IPA, nBu_4NOAc,90°C, olefin

Avecia

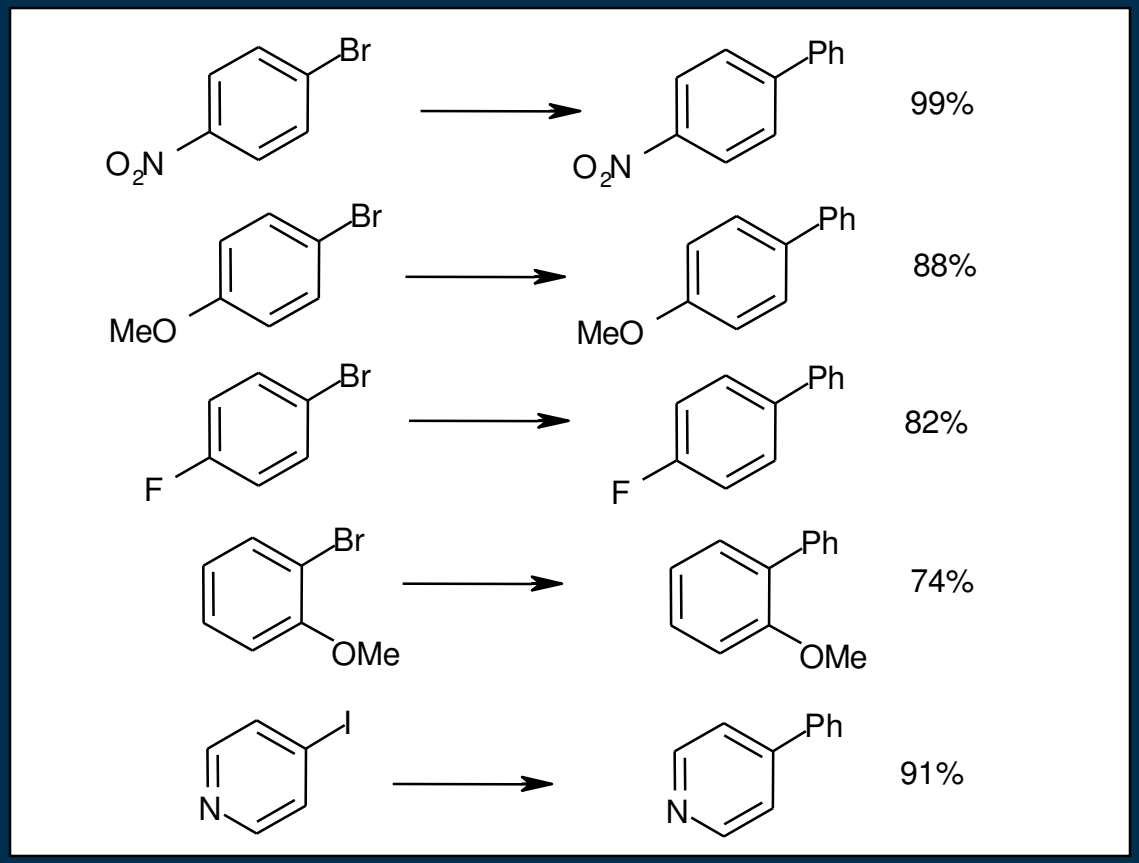
Pd EnCat™ 40 Catalysed Carbonylations

Substrate	Product	Yield (%)
		89
		99
		95
		93
		98

Conditions: 3mol% Pd EnCat™ 40, nBuOH, CO, TEA, 90°C

Avecia

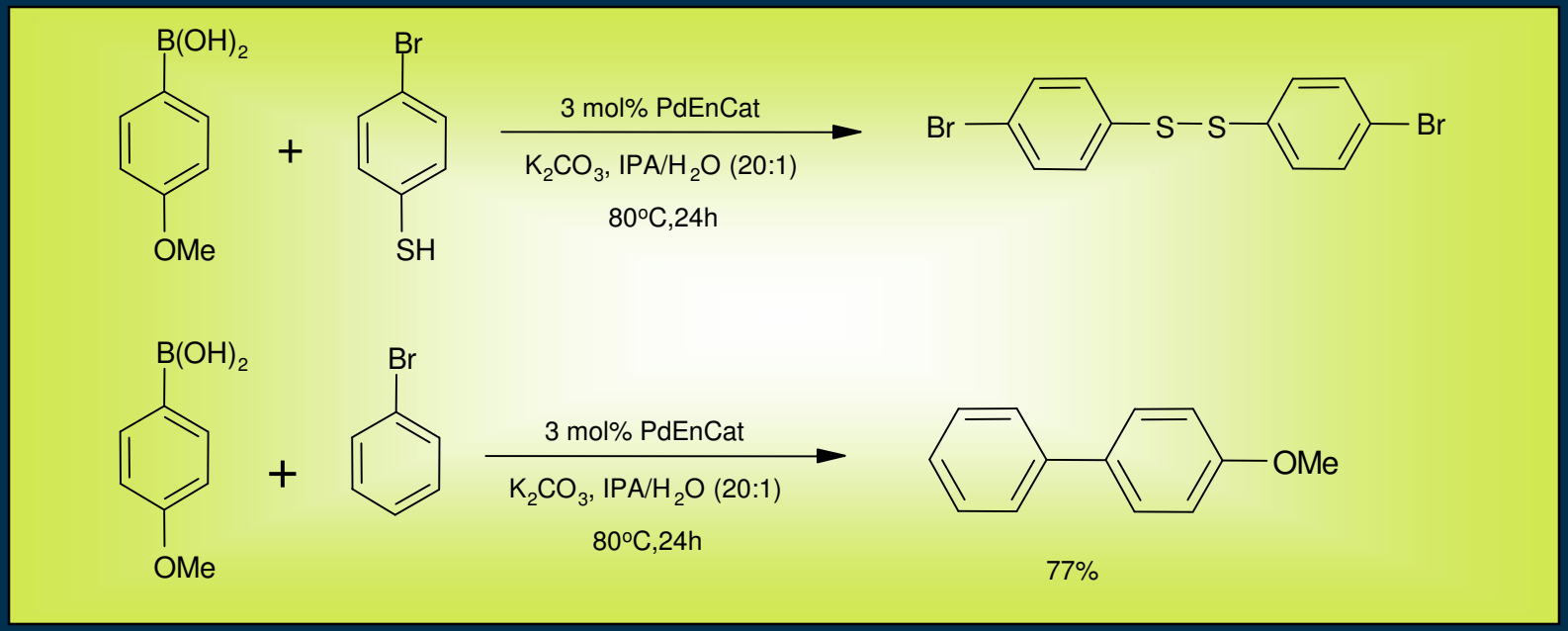
Pd EnCat™ 40 Catalysed Stille Reactions



Conditions: 2.5mol% Pd EnCat™ 40, IPA/Tol 1/1, nBu_4NOAc, 90°C, Me_3SnPh

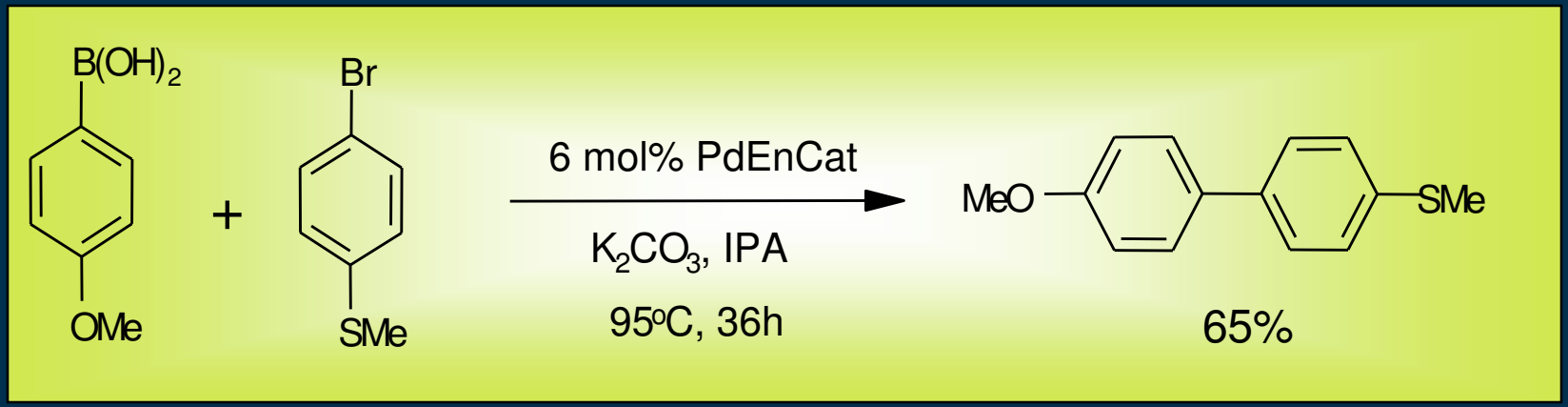
Avecia

Influence of Thiol Substrates In Pd EnCat™ Suzuki Couplings



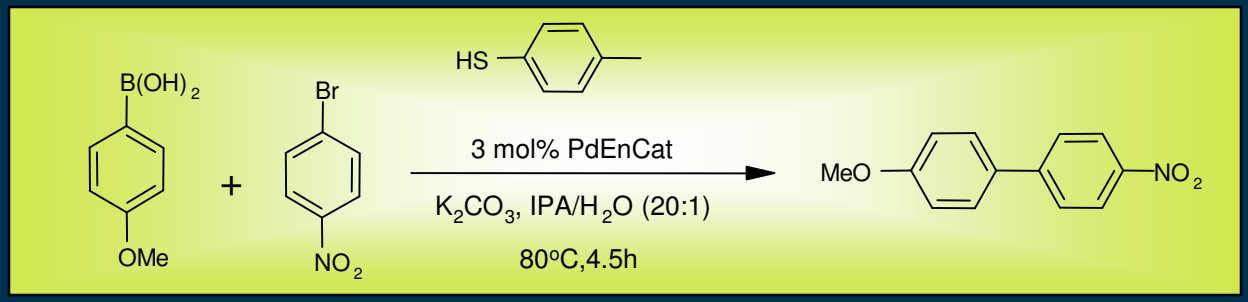
Avecia

Pd EnCat™ 40 Suzuki Coupling of Sulfides



Avecia

Pd EnCat™ 40 & Suzuki Coupling In the Presence of Thiol Contaminant



4-THIOCRESOL	45min	2.5h	3h	4h	Crude
0%	66%	82%	82%	82%	>90% (5h)
0.1%	37%	73%	79%	81%	>90% (5h)
1%	1%	1%	-	3%	3% (24h)
3%	1%	2%	-	4%	4% (24h)

Avecia

Hydrogenation and Transfer Hydrogenation with Pd(0) EnCat™ and Pd(0) EnCat™ NP

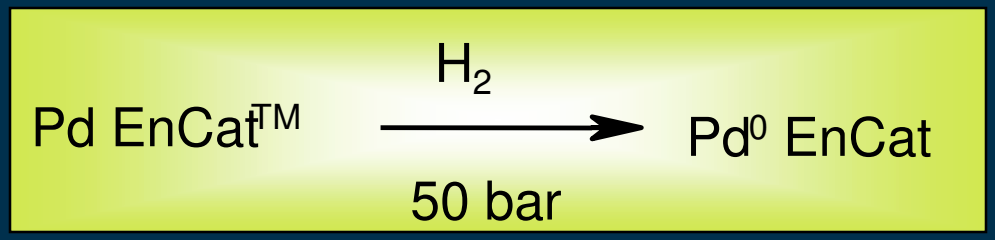
- Pre activation of catalyst required:

  Reduction of Pd with hydrogen

  or

  Reduction of Pd with formic acid

Characteristics Pd(0) EnCat™



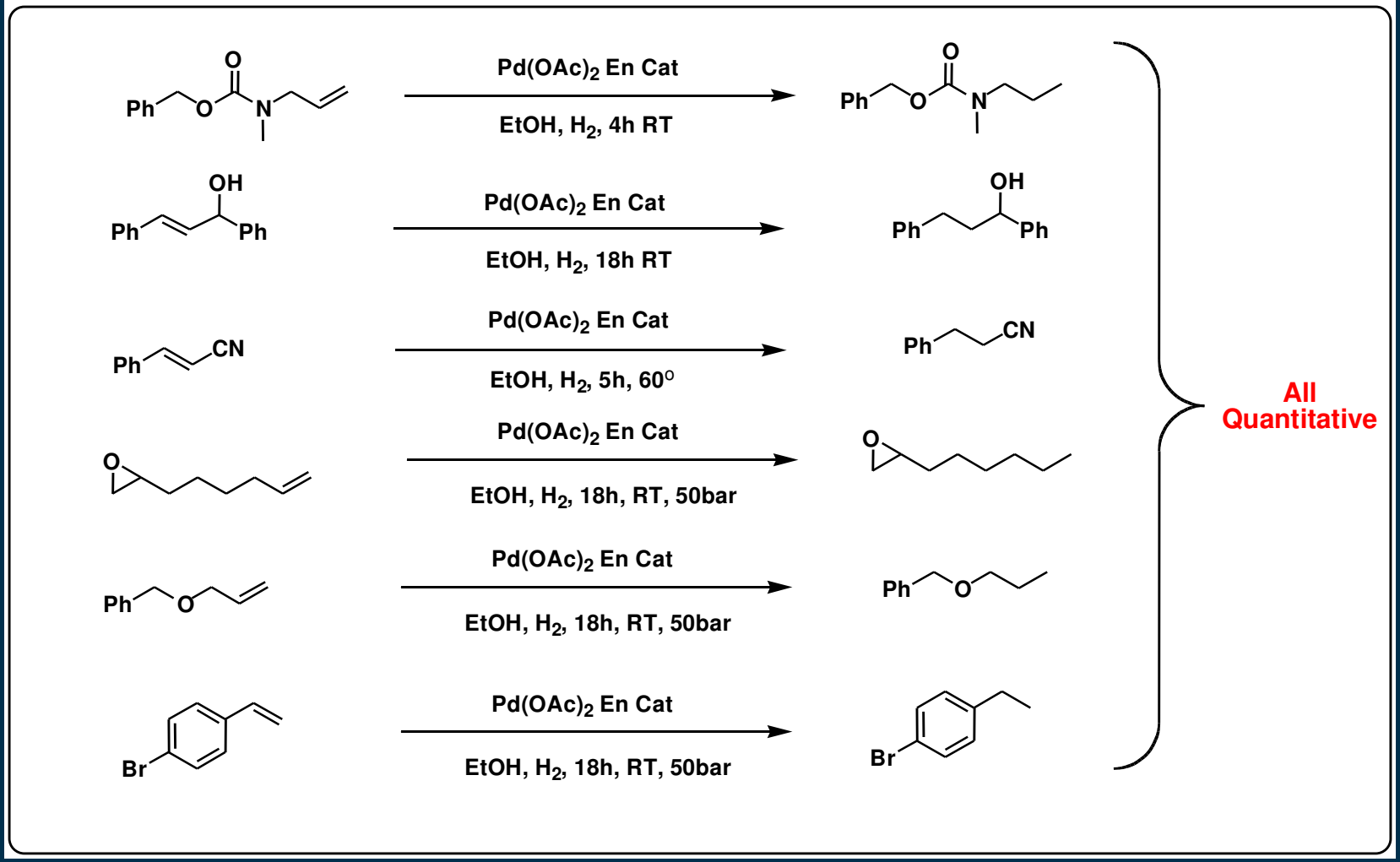
Low activity catalyst

Pd Particles > 5nm, single domain and well ordered

Selective reductions possible

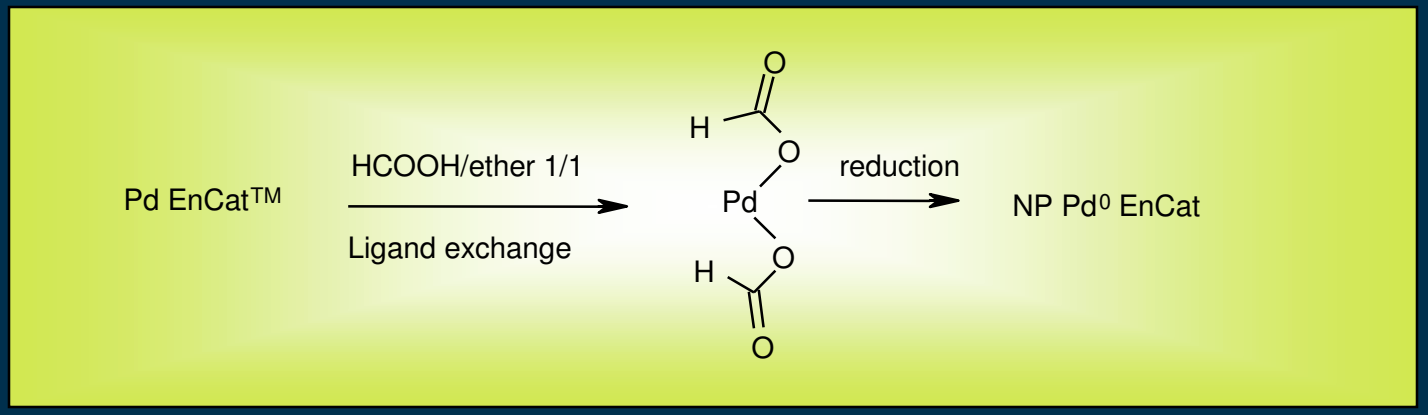
Pd(0) EnCat™ 40 Hydrogenations

Pd(OAc)$_2$ En Cats in Hydrogenation



Avecia

Preparation of Nano Particulate Pd(0) EnCat™ NP

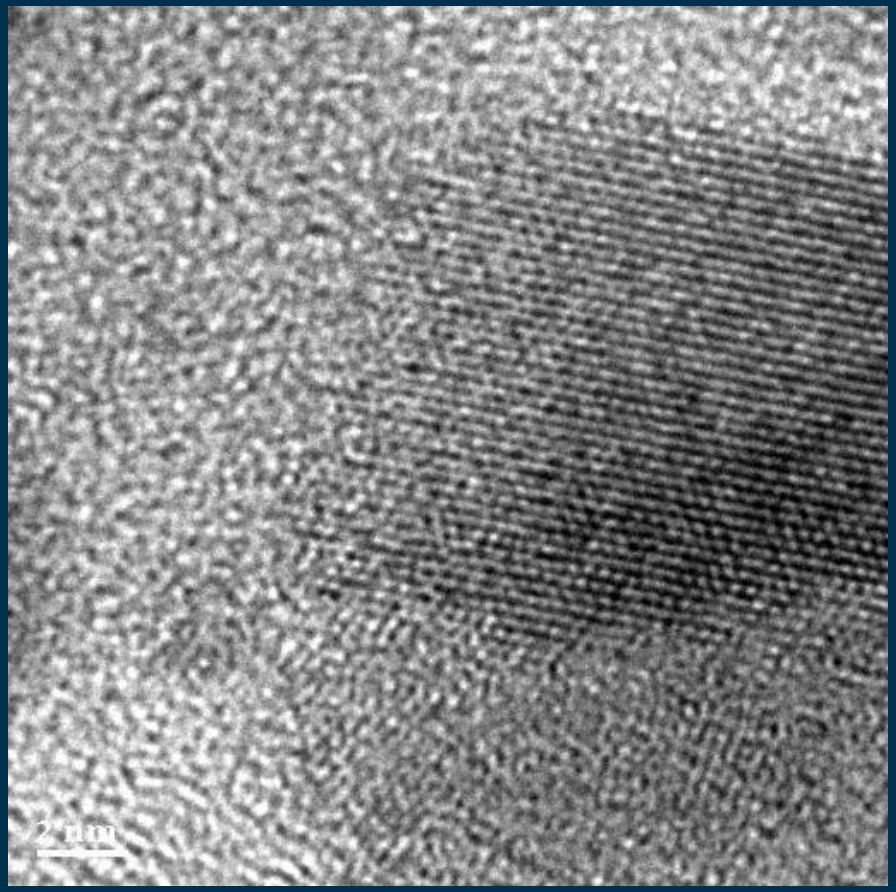


Pd particles <2nm (approx 10 atoms)
Nano structure stabilised by polyurea matrix

Highly active and recyclable H_2 transfer catalyst
High chemoselectivity
Non pyrophoric

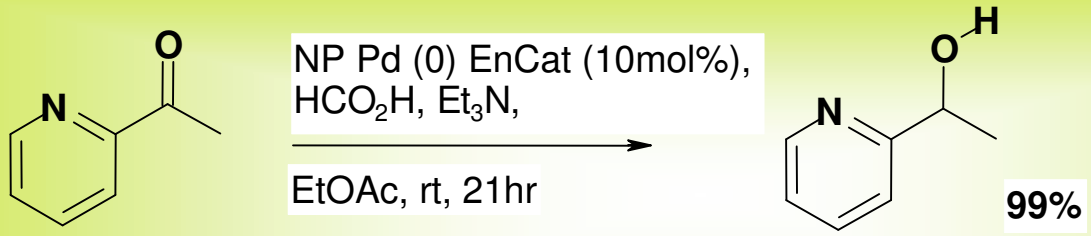
Avecia

Nano Particulate Pd(0) EnCat™ NP



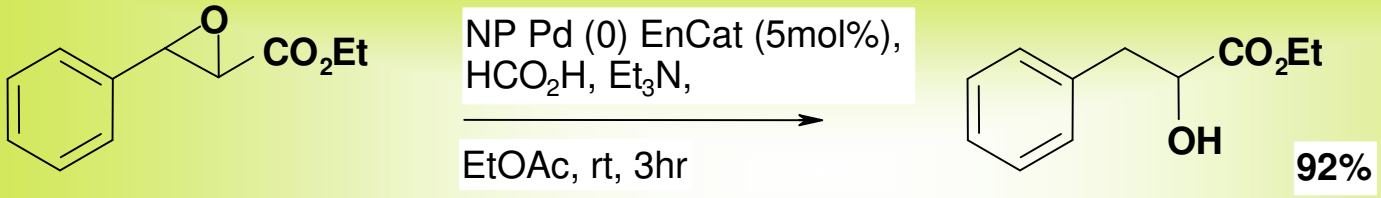
Avecia

Transfer Hydrogenation with Pd(0) EnCat™ 40NP



Ley, S.V.; Ramarao, C.; Yu, J-Q.; Wu, H-C.; Spencer, J., *Chem Commun.*, **2003**, 678-679

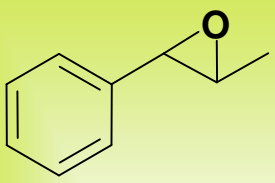
Smith S. C., *Speciality Chemicals,* in press, Sep **2004**.



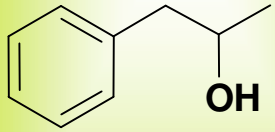
Ley, S.V.; Mitchell, C.; Pears, D.; Ramarao, C.; Yu, J.-Q.; Zhou, W., *Org. Lett.,* **2003**, *5(24),* 4665-4668.

Avecia

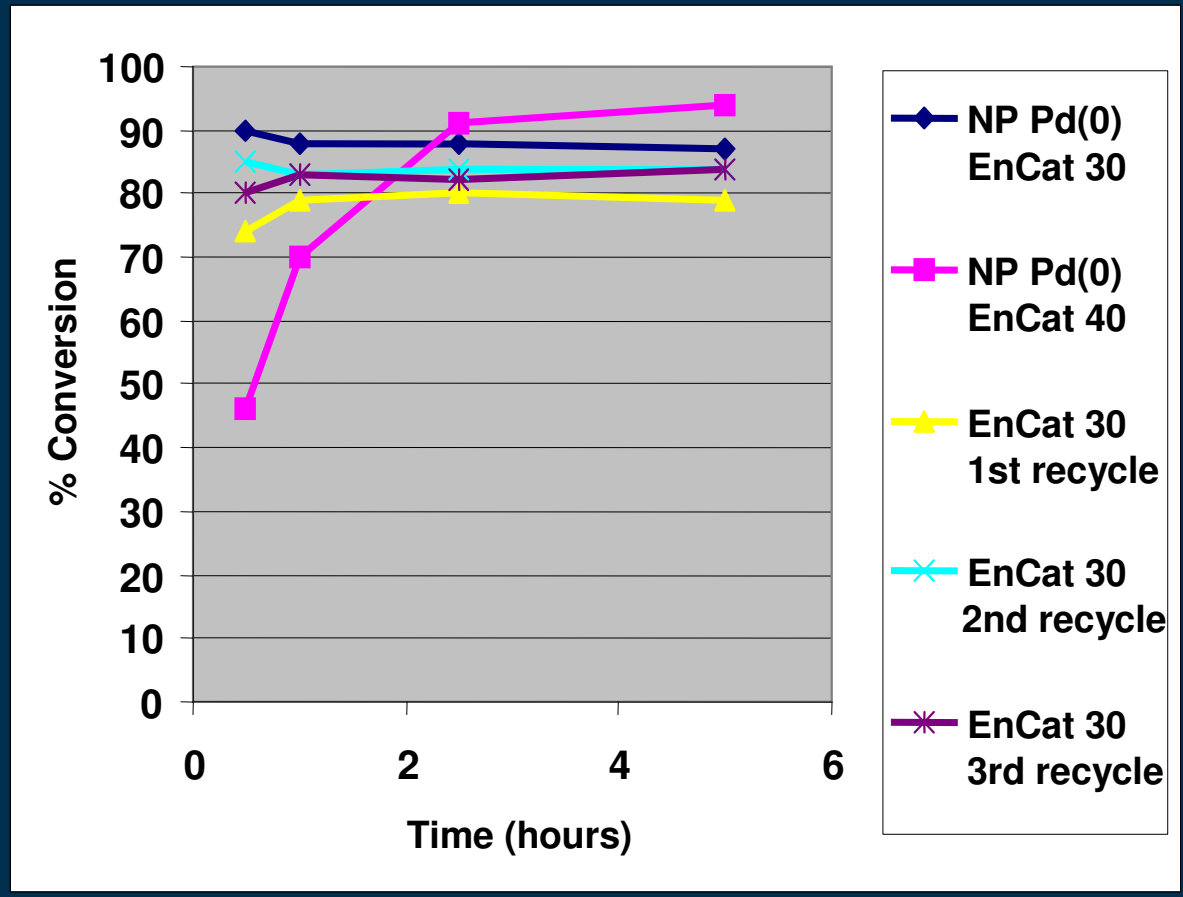
Kinetics Pd(0) EnCat™ 40NP vs Pd(0) EnCat™ 30NP



5 mol% catalyst
HCO_2H (4 eq)
Et_3N (4 eq)
EtOAc

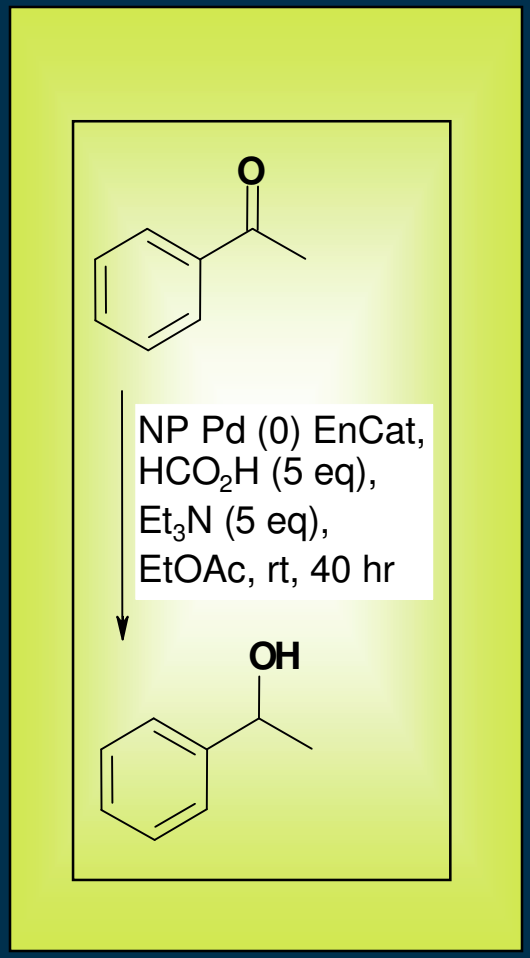


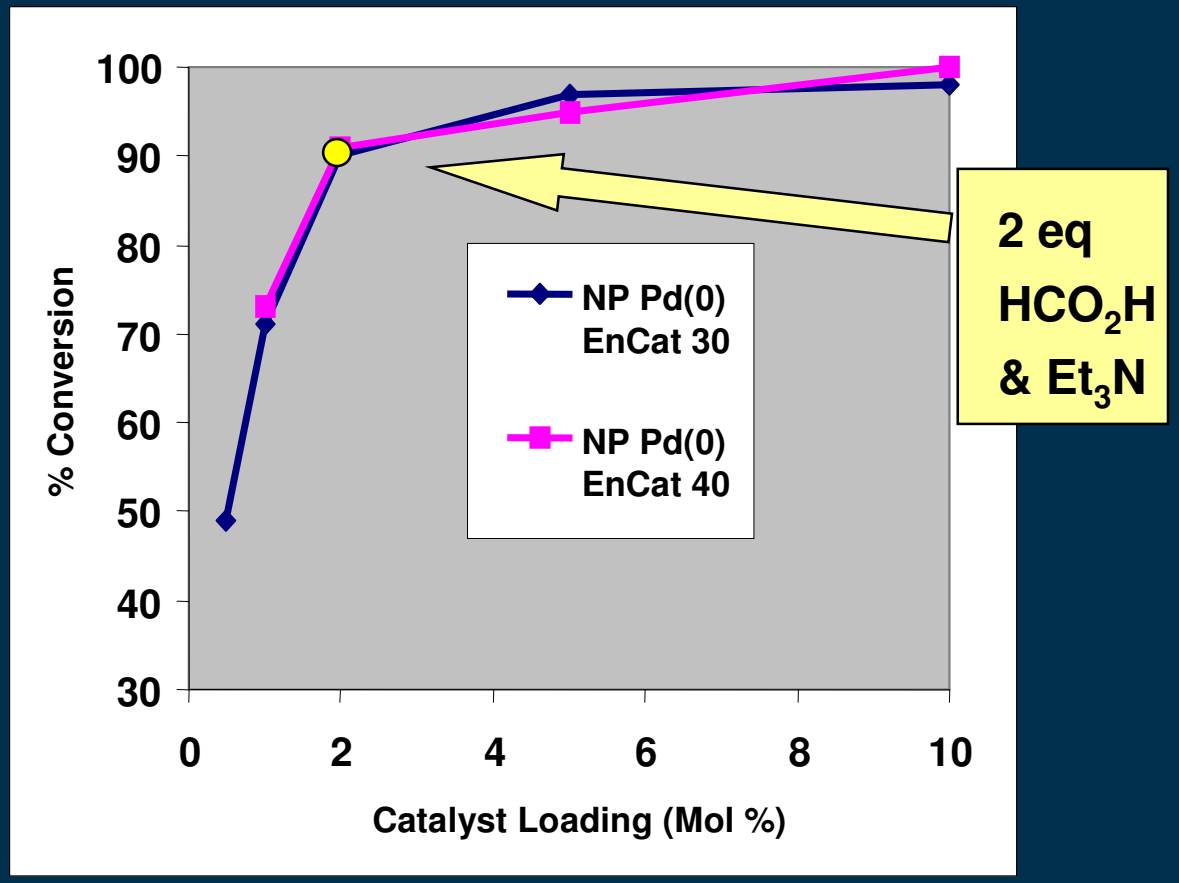
<1ppm Pd in reaction solution



Avecia

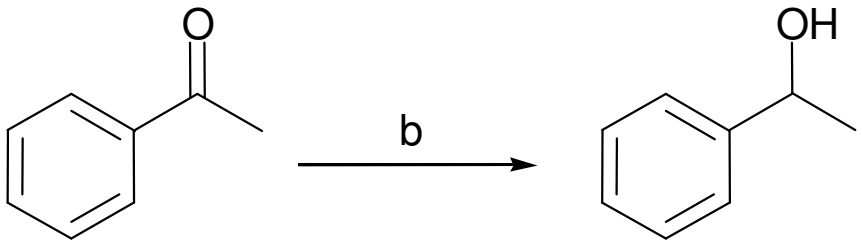
Transfer Hydrogenation of Aryl Ketones – Catalyst Loading Study





Avecia

Recycle - Transfer Hydrogenation of Aryl Ketones with Pd(0) EnCat™ 40NP

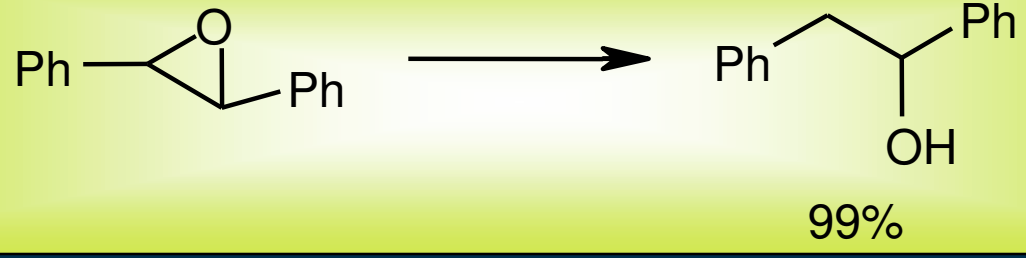


Run	1	2	3	4	5
Yield (%)	99	98	98	97	96
Time (h)	21	22	24	26	28

[b] *Reagents and conditions*: 10 mol% NP Pd^0 EnCat, 200 µL EtOAc, 0.8 mmol HCOOH, 0.8 mmol Et_3N, 0.16 mmol acetophenone, 24 ºC.

Avecia

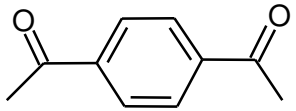
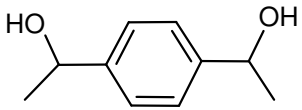
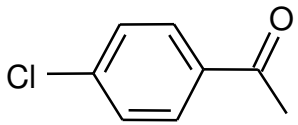
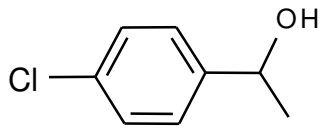
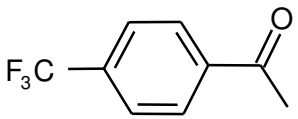
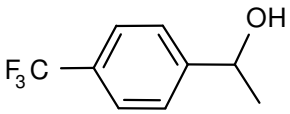
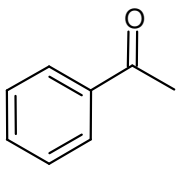
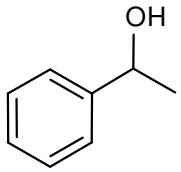
Recycle - Transfer Hydrogenation of Benzylic Epoxides with Pd(0) EnCat™ 40NP



Conditions: 5 mol% NP Pd^0 EnCat™, Et_3N, HCOOH, EtOAc, 5 hours

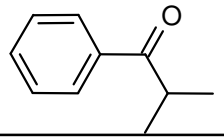
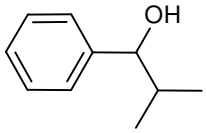
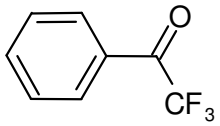
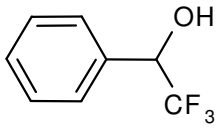
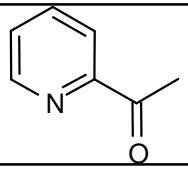
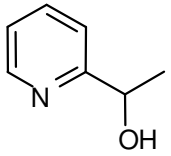
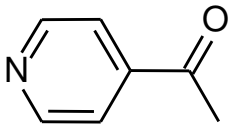
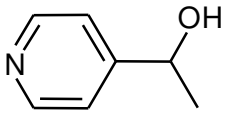
Catalyst recycled 10 times without loss of activity or yield

Transfer Hydrogenation of Aryl Ketones with Pd(0) EnCat™ 40NP

Substrate	Product	Time (hr)	Yield (%)
		68	99
		48	95
		24	92
		21	99

Avecia

Transfer Hydrogenations
Aryl Ketones with Pd(0) EnCat™ 40NP

Substrate	Product	Time (hr)	Yield (%)
		36	90
		48	99
		18	99
		18	99

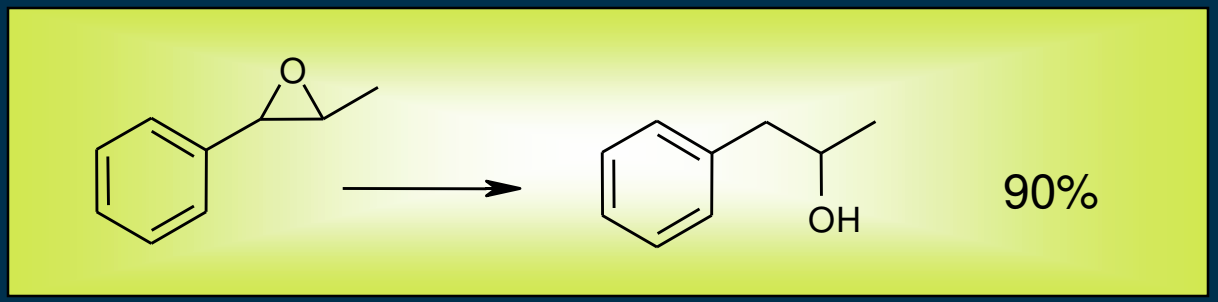
Avecia

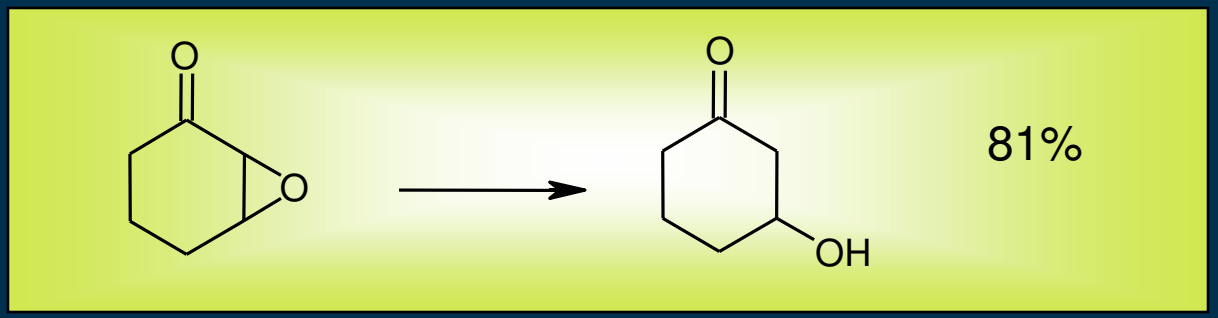
Chemo-selective Transfer Hydrogenation Of Nitro Groups with Pd(0) EnCat™ 40NP

Conditions: 10 mol% NP Pd^0 EnCat™, EtOAc, HCOOH, Et_3N, Ketone, RT

Avecia

Transfer Hydrogenation of Benzylic Epoxides by Pd(0) EnCat™ 40NP

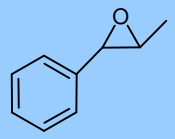
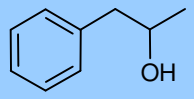
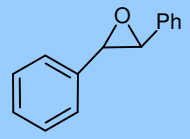
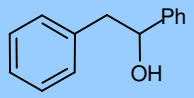
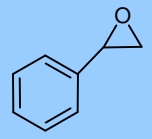
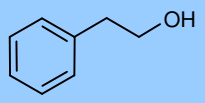
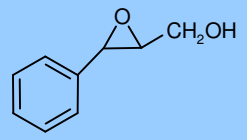
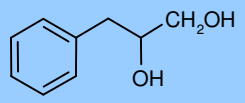
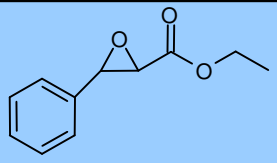
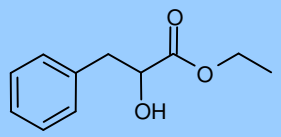




Conditions: 5 mol% Pd EnCat™, Et_3N, HCOOH, EtOAc, 3 hours

Avecia

Transfer Hydrogenation Of Benzylic Epoxides with Pd(0) EnCat™ 40NP

Substrate	Product	Time (h)	Yield (%)
		3.5	90
		5.5	97
		5	72
		4.5	92
		12.5	92

Avecia

Transfer Hydrogenation Of Benzylic Epoxides with Pd(0) EnCat™ 40NP

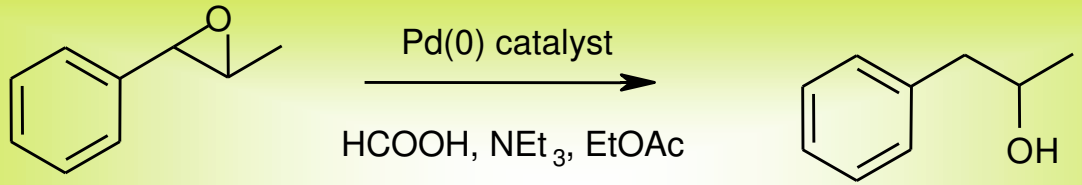
99%

Conditions: 5 mol% NP Pd^0 EnCat™, Et_3N, HCOOH, EtOAc, 5 hours

Catalyst recycled 10 times without loss of activity or yield

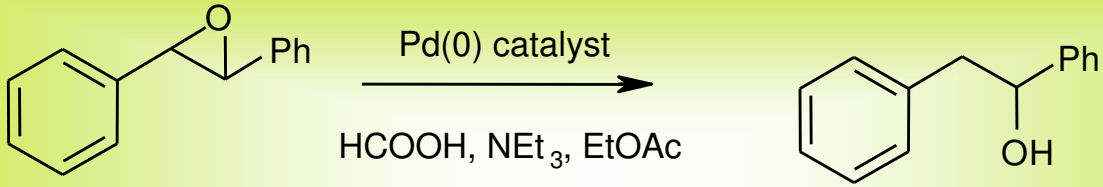
Avecia

Transfer Hydrogenation - Comparison of Pd(0) EnCat™ 40NP with Pd/C



10% Pd/C (5 mol%) - 48%

Pd EnCat™ (5mol%) - 90%

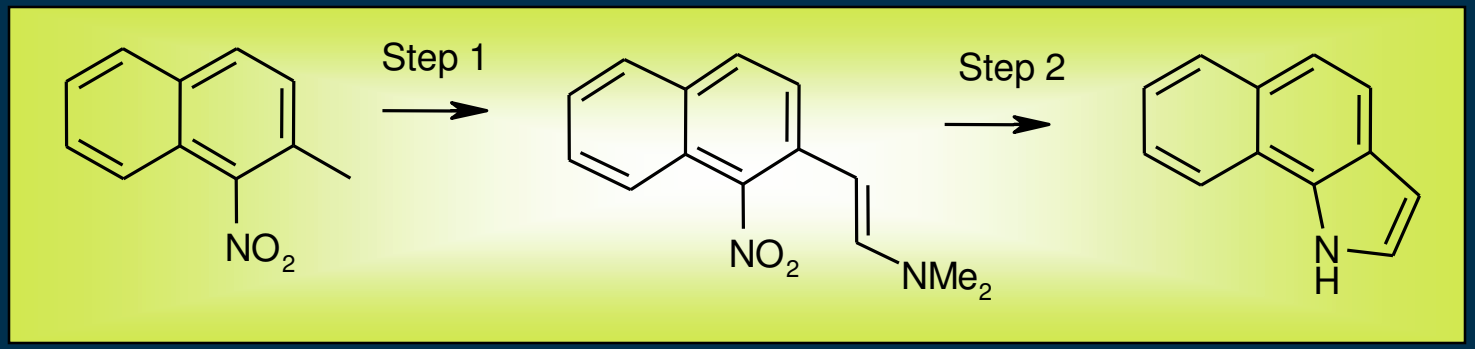


10% Pd/C (5 mol%) - 80%

Pd EnCat™ (5mol%) - 97%

Avecia

Reductive Cyclisation to Indole by Pd(0) EnCat™ 40NP



Step 1 Leimgruber-Batcho – microwave, DMF, Lewis acid

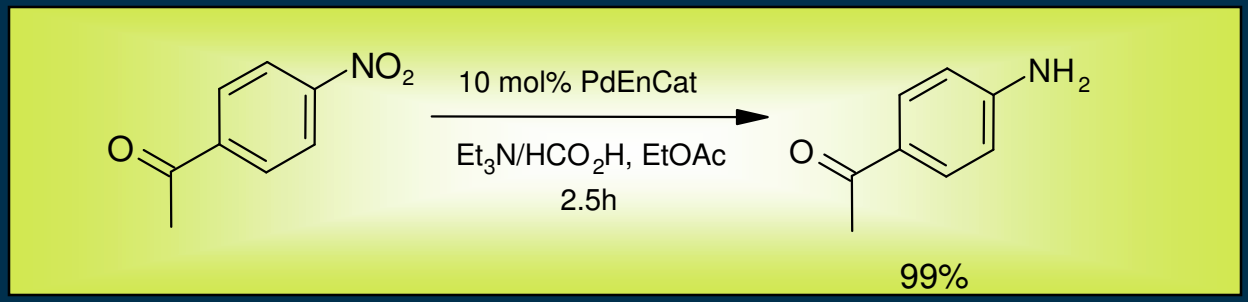
Step 2 6 mol% NP Pd^0 EnCat™, EtOAc, 5 equiv $HCOOH/Et_3N$, 24°C, 24 hours

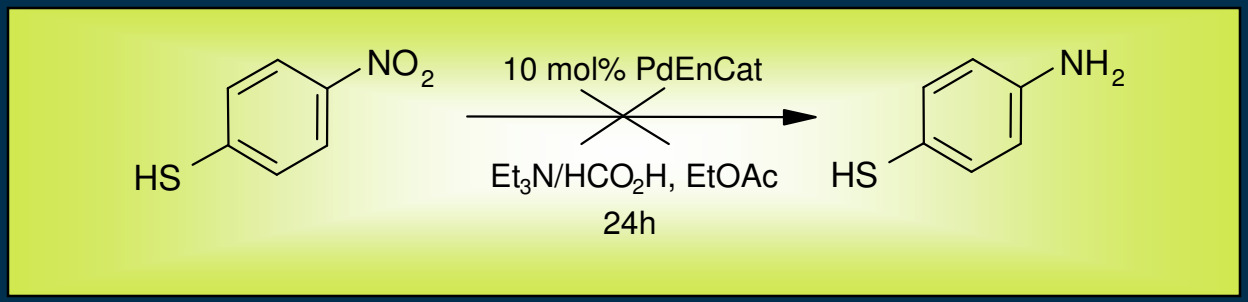
or

microwave, 120°C, 2 hours

Avecia

Influence of Thiol Substrates in Pd(0) EnCat™ 40NP Transfer Hydrogenation Of Nitro Groups





Avecia

Advantages of Pd(0) EnCat™ 30NP

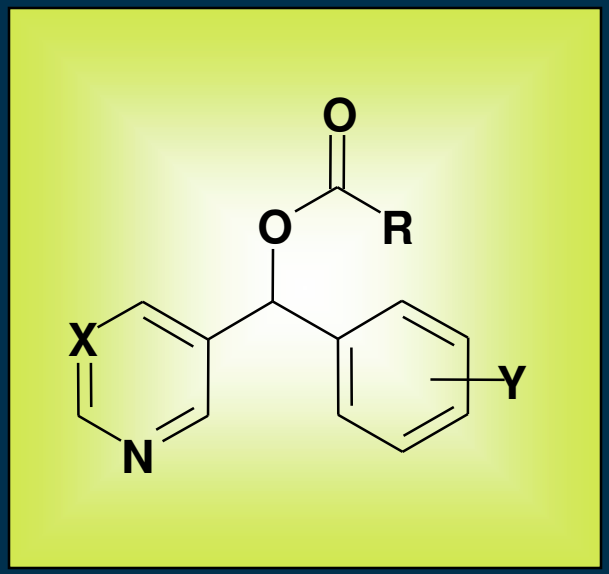
- Easy and safe to handle vs Pd/C
- Hydrogenations without the need for hydrogen gas
- Simple recovery of catalyst
- Very low metal contamination
- Versatile matrix
- Can be recycled

Avecia

Pd EnCat™ in Parallel Synthesis

Avecia

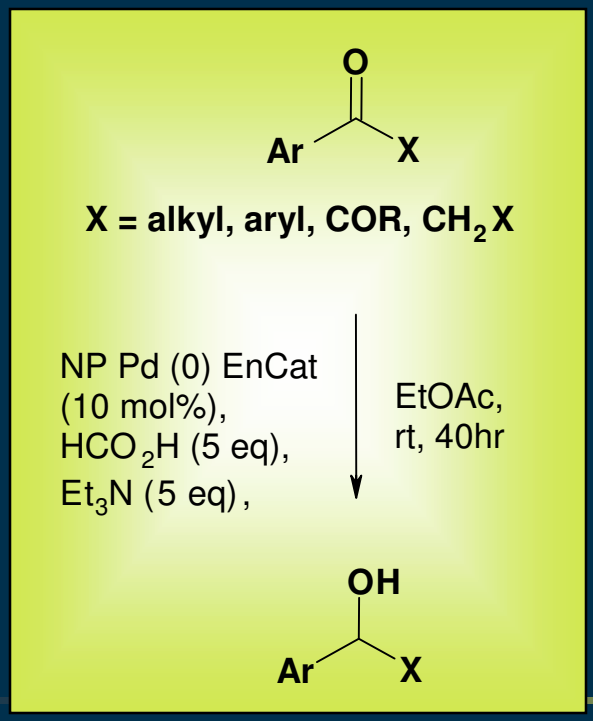
Automated Library Synthesis with Pd(0) EnCat™ 40NP



- O-capped biaryl carbinols of interest as herbicides
- Can we use Pd^0 EnCat to prepare a range of alcohol intermediates in a library synthesis?
- Building blocks would be of general use in other chemistries

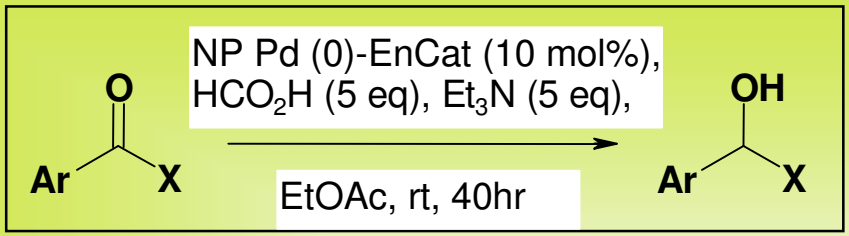
Parallel Substrate Screening Experiment

- Use of 2 x 48 Bohdan Miniblocks for scale and ease of filtration
- Evaporated filtrate + DCM + water filtered through phase separation plate
- 96 products analysed by LC-MS, GC-MS and NMR

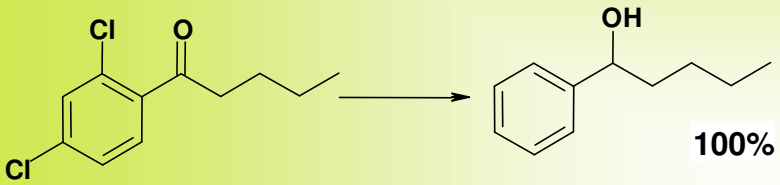


Avecia

Examples of Successful Reactions



Reduction of a range of aryl ketones proceeded cleanly:



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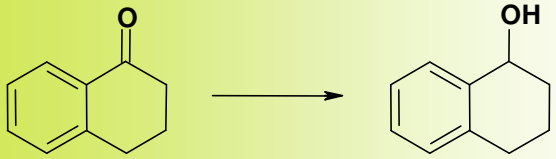
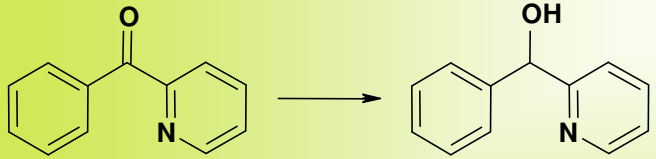
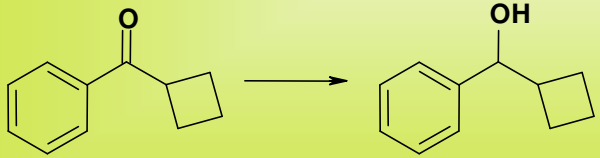


83%



79%



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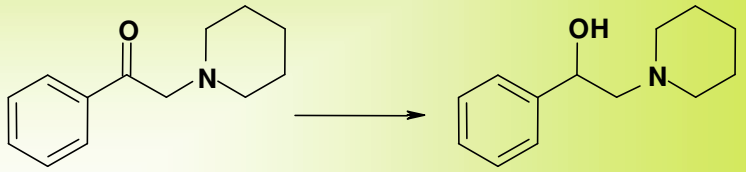
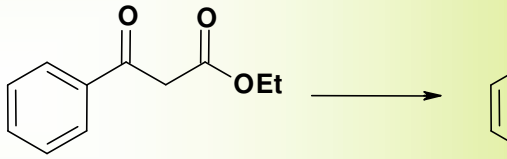


94%



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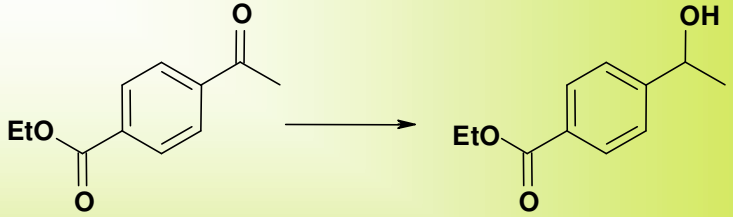

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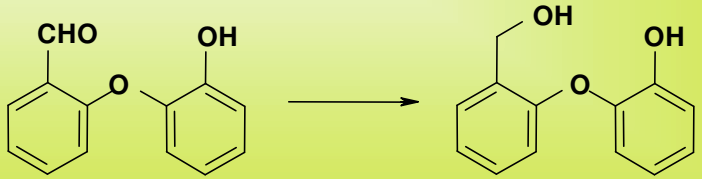
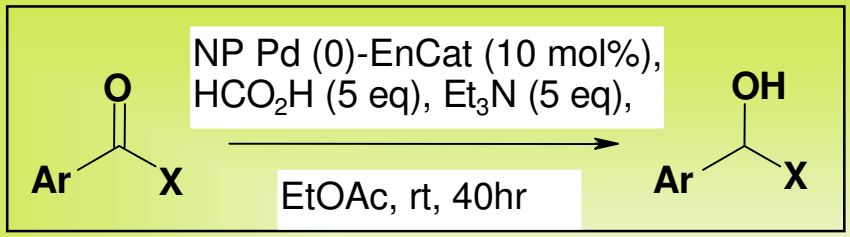
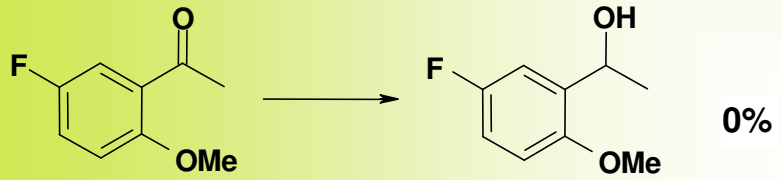


100%

Examples of Low Yield Transfer Reductions with Pd(0) EnCat™ 40NP



Aryl electronics and sterics have the greatest influence on reactivity:



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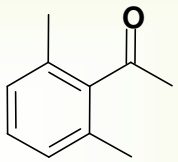

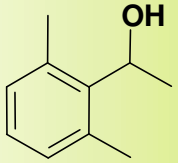

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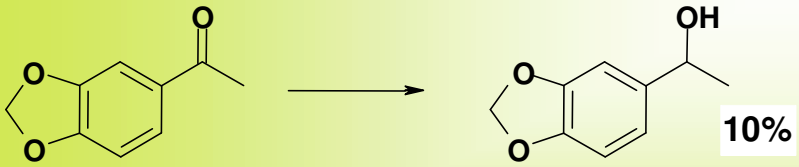
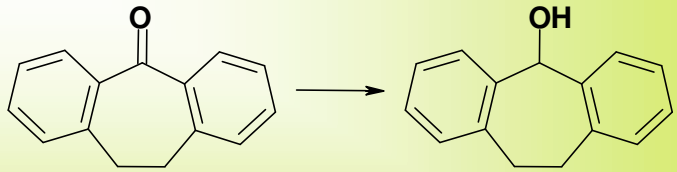
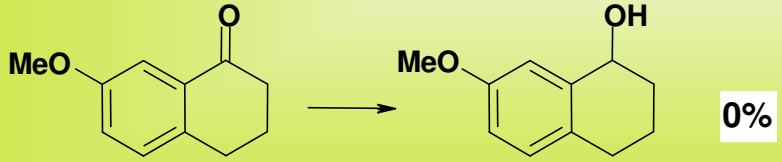


10%



15%
+ 10% CH_2



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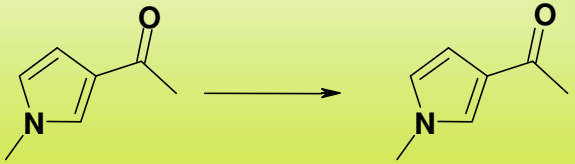

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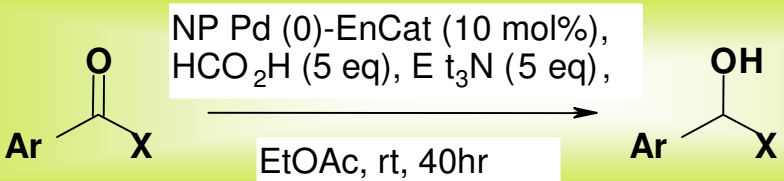
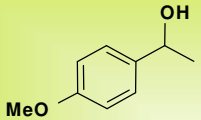
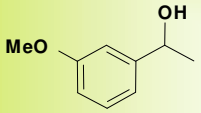
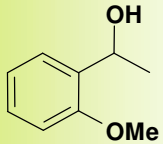
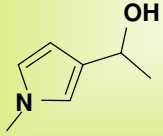
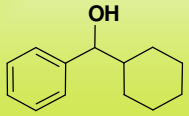
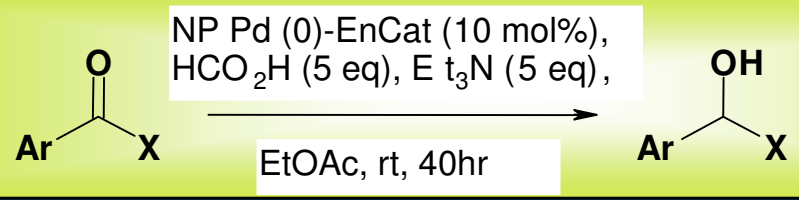
Influence of Switching to Pd(0) EnCat™ 30NP with Difficult Substrates

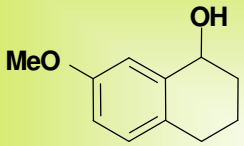
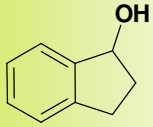
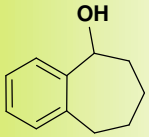
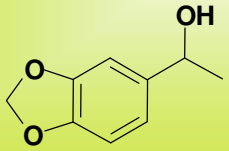


	NP Pd ^{0} EnCat 40	NP Pd ^{0} EnCat 30
	28	54
	50	75
	4	13
	0	2
	55	93

Avecia

Influence of Switching to Pd(0) EnCat™ 30NP with Difficult Substrates



	NP Pd^0 EnCat 40	NP Pd^0 EnCat 30
	<5	20
	33	60
	18	22
	10	29

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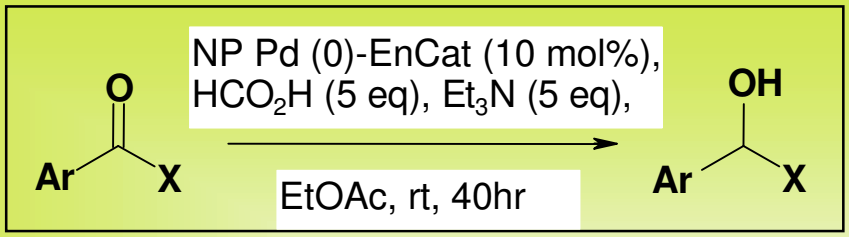
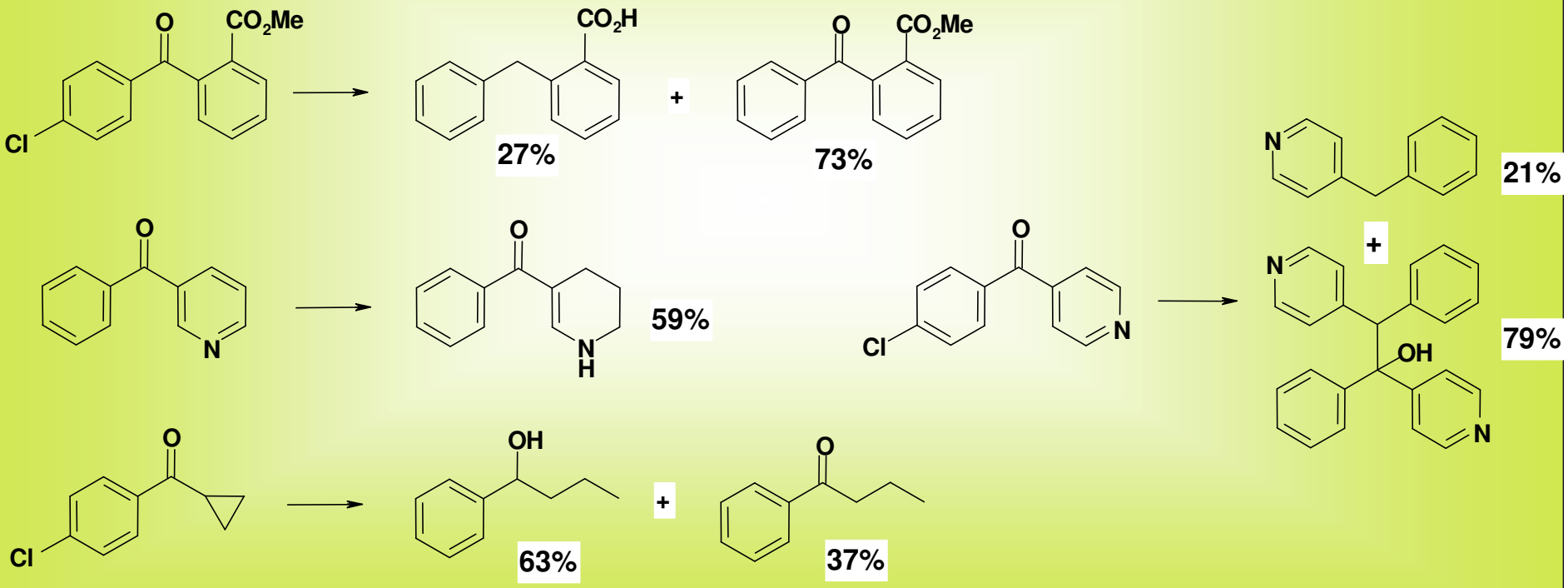
Unusual Products



Alternative reduction products:



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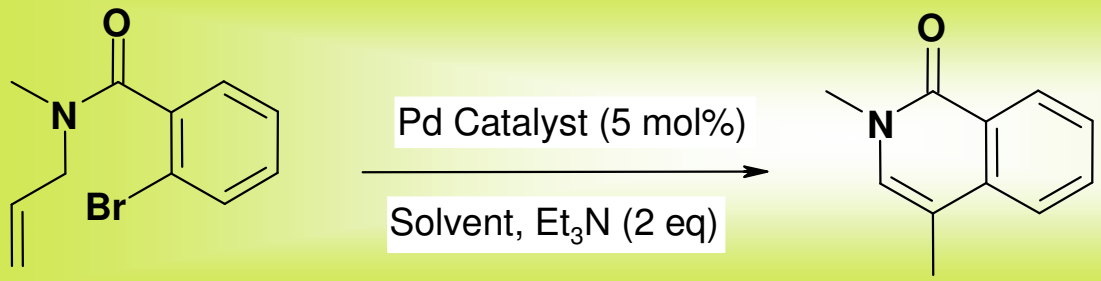
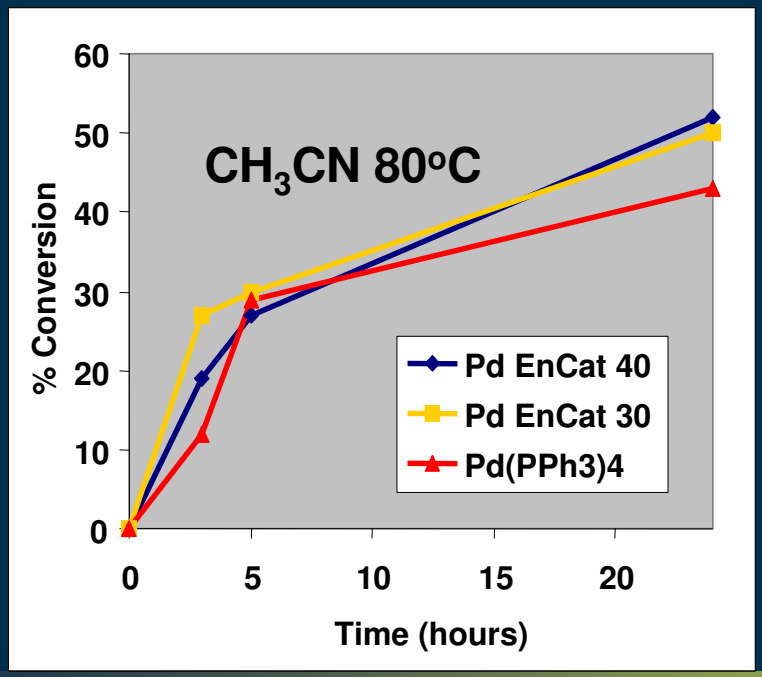
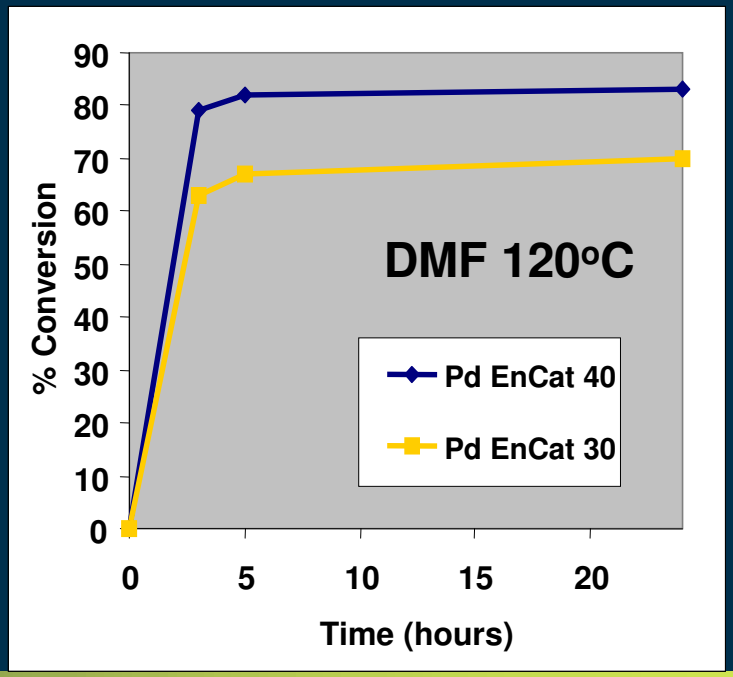
Intramolecular Heck Library: Pd EnCat™ 30 vs 40



Use of Zinsser Sophas for top filtration of catalyst





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Process Case Studies with Pd EnCat™

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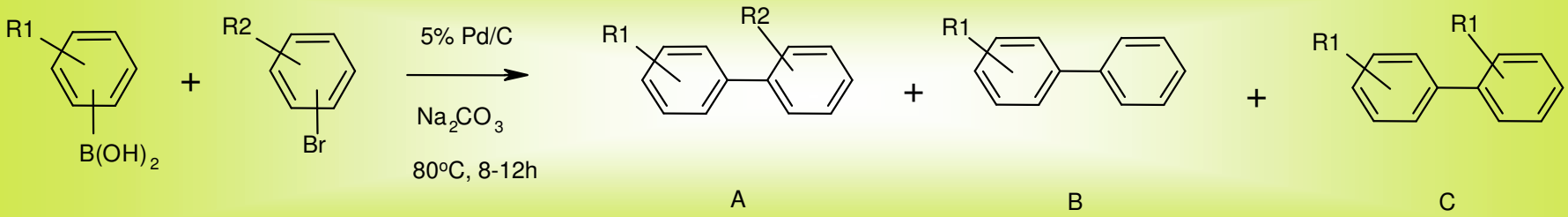
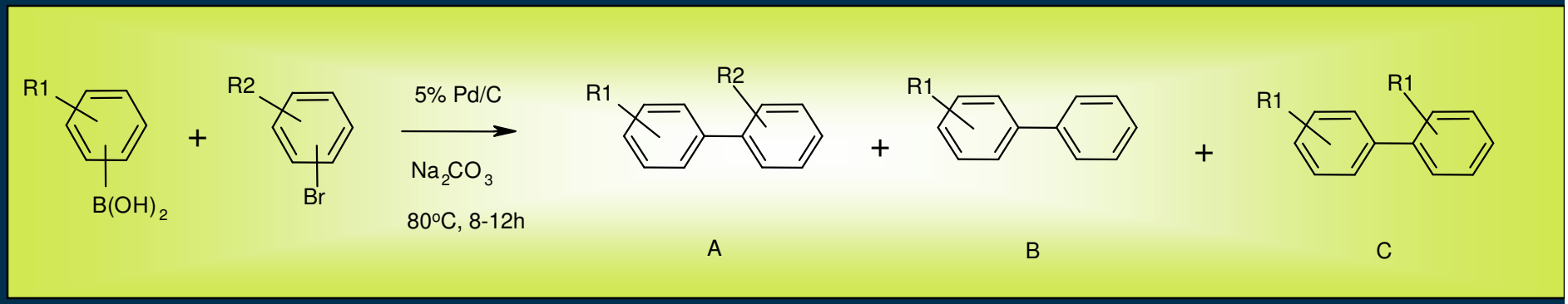
Suzuki Coupling Process Example
Pd EnCat™ 30 vs 5% Pd/C



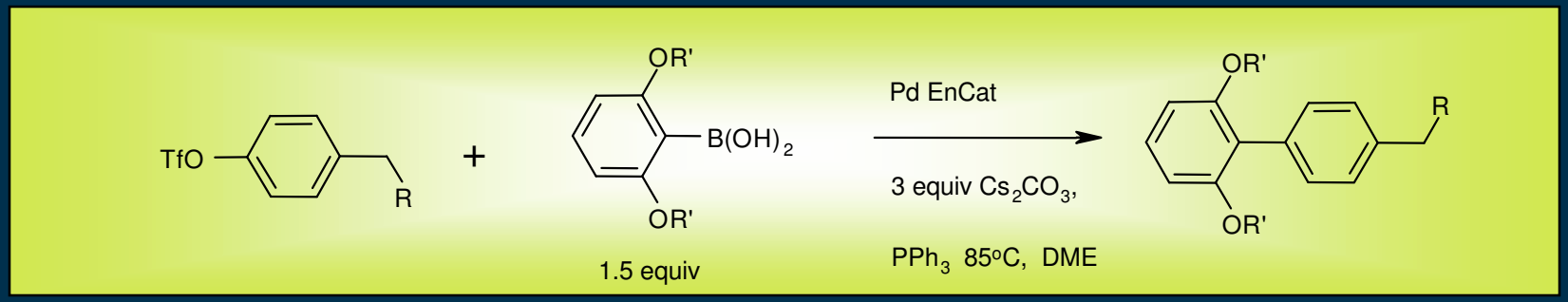
5% Pd/C 2.5mol%	30min	87	13	0
	60min	94	5	1
EnCat 30 2.5mol%	30min	97	<1	<1
1.25mol%	30min	>99	<1	<1
0.5mol%	30min	>99	<1	<1
0.05mol%	30min	>99	<1	<1

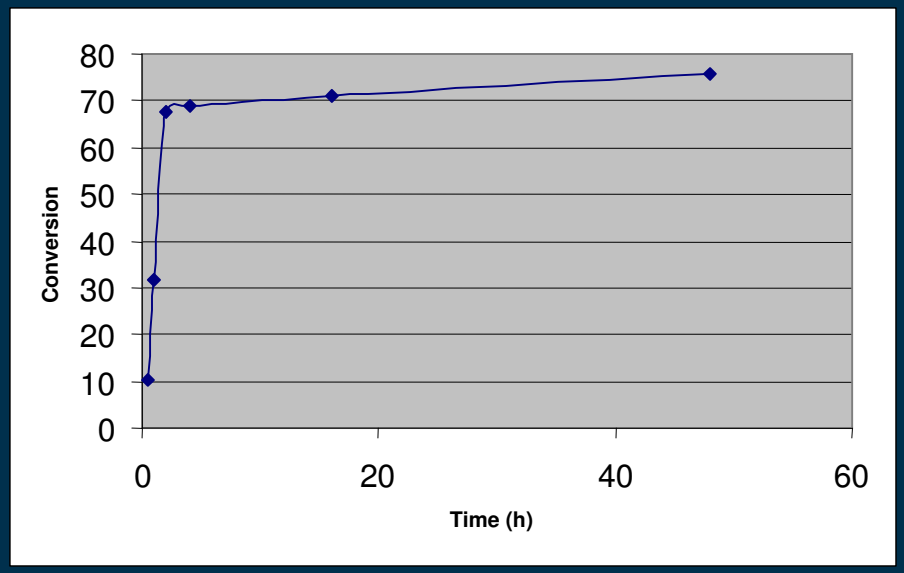
Suzuki Coupling Process Example
Pd EnCat™ 30 vs 5% Pd/C



		% Yield A	Pd (ppm) in crude product
5% Pd/C 2.5mol%	60min	94	56
EnCat 30 1.25mol%	30min	>99	14
0.5mol%	30min	>99	23
0.05mol%	30min	>99	9

Hindered Suzuki Process E.g. – Problem Residual Pd with Homogeneous Catalyst $PdCl_2(PPh_3)_2$





<50ppm Pd in crude product

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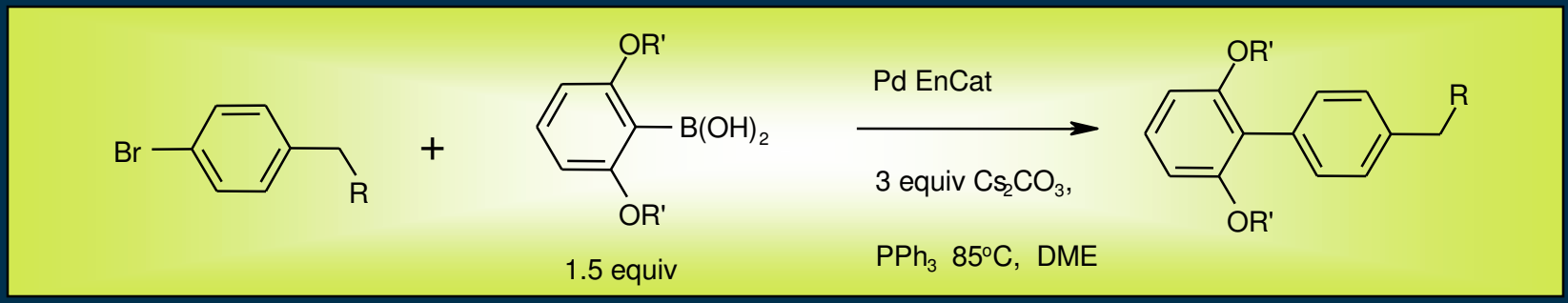
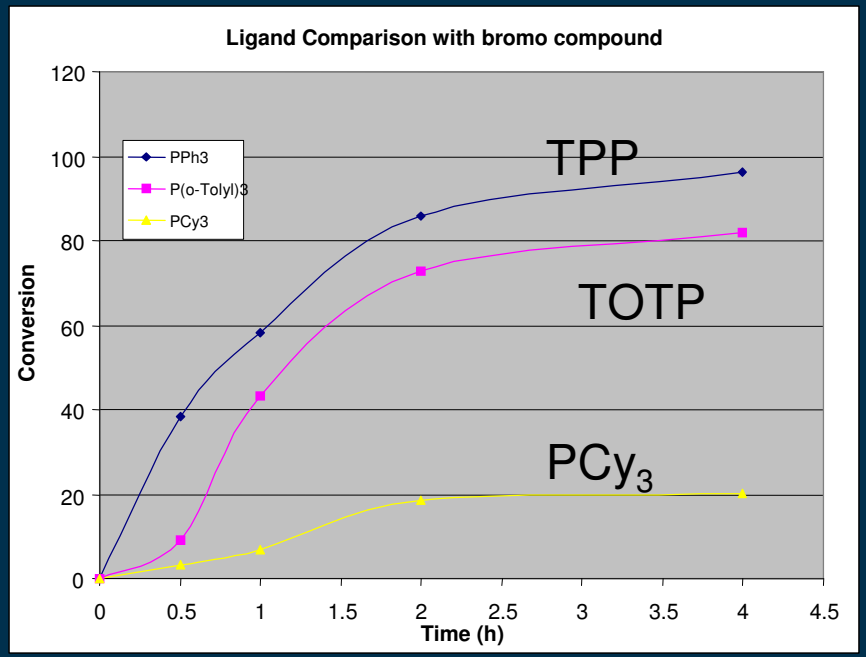
Hindered Suzuki Process E.g. – Problem Residual Pd with Homogeneous Catalyst $PdCl_2(PPh_3)_2$





<15ppm Pd in crude product

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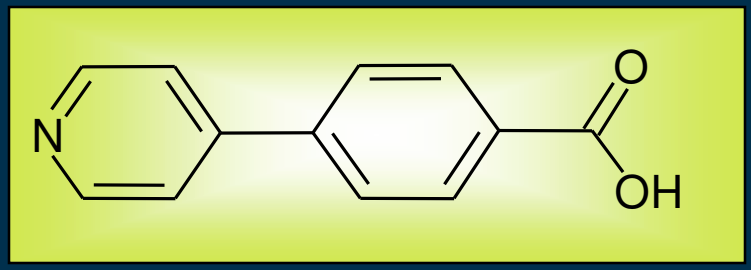
Case Study - Pd EnCat™ 40

Suzuki Coupling Route

to 4-Pyridin-4-yl-benzoic acid:



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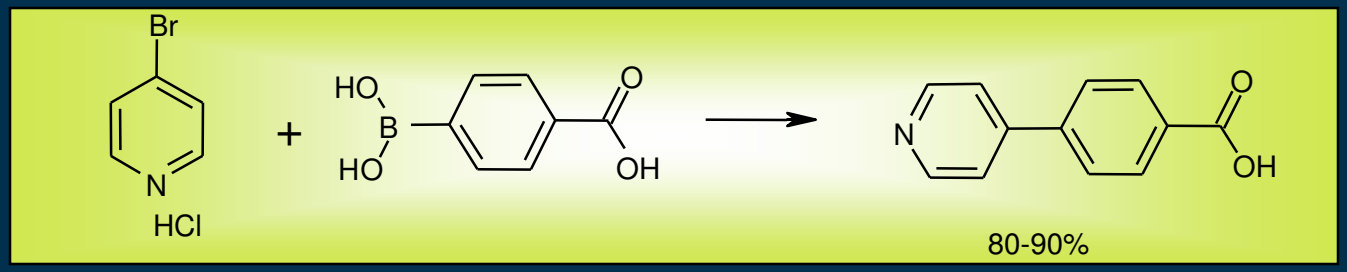
Existing Homogeneous Route



Conditions: EtOH/Water, K_2CO_3, Ligand, 0.4-1 mole% Pd $(PPh_3)_4$

Issues:

- 600ppm Pd in crude product
- Pd in waste stream
- Cost - no catalyst reuse

Target to achieve <100ppm Pd in crude

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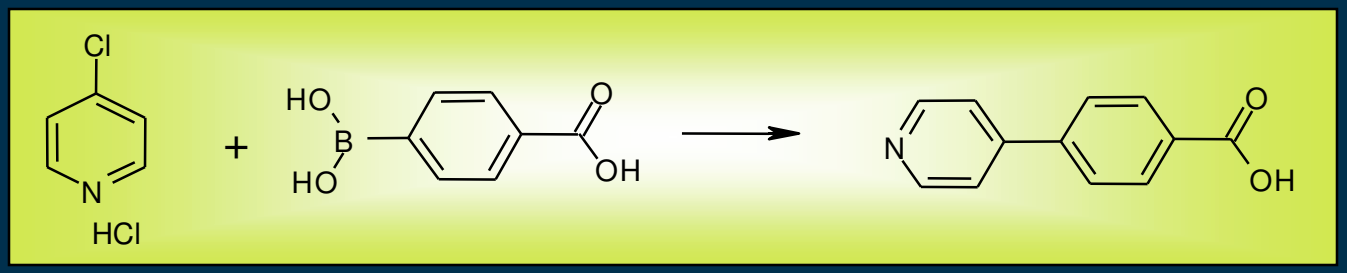
Pd EnCat™ 40 Case Study

- No reaction without addition of phosphorus ligand
- 0.75 mole % Pd EnCat™ 40, 2.5 mole % TPP
- 75-85 % yield
- Reuse >3x without loss of activity
- Only 20ppm Pd in waste stream
- But 400ppm Pd in crude product (2 to 4% loss)

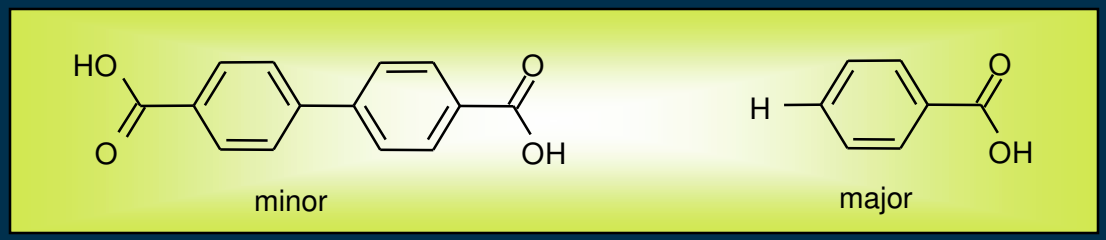
Pd EnCat™ 40 Case Study

Changed to much cheaper chloro pyridine:



No product under previous conditions Pd EnCat™ 40 / TPP

Extensive ligand screen – monitoring yields and impurity profiles:



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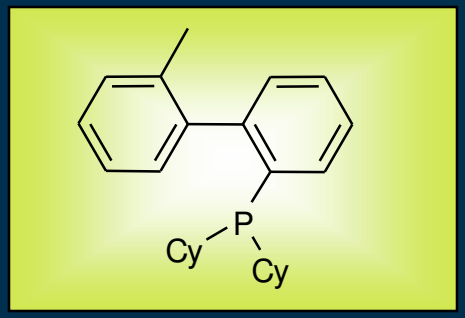
Pd EnCat™ 40 Case Study

Biphenyl phosphines best ligands:



Highly active catalyst, optimisation reduced both Pd and ligand charge versus bromopyridine reaction:

Ligand: 0.3 mole% biphenyl vs 2.5 mole% for TPP

Pd EnCat™: 0.13 mole% Pd vs 0.75 mole%

Rate x3 faster than bromopyridine

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Pd EnCat™ Optimised Process

- 85% product yield
- Successful scale up

  - easy to charge & filter catalyst with low cake resistance
  - good mixing with retreat curve impellers

- Rate acceleration for Pd EnCat™ x30 that of $Pd(OAc)_2$*
- Catalyst recycle
- 90 ppm Pd in crude product – achieving 100ppm customer target.
- Remove catalyst & reaction stops, implies reaction occurs within EnCat™ matrix

** Reaction in beads provides an area of localised high catalyst/reagent concentration?*

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Pd EnCat™ - Reported Benefits at Process Scale

- no plating out of palladium metal on vessel walls
- reduced cleaning issues; reducing solvent use and cycle time
- ability to access a wider range of process technology e.g. fixed bed, fluidised, trickle bed and microwave reactors
- safer to handle vs palladium on carbon
- reduced metal loss
- integrates into standard chemical plant

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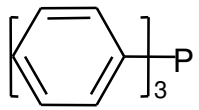
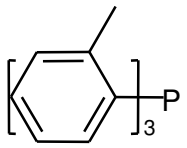
Acknowledgments

Avecia	Cambridge	Syngenta	AstraZeneca
D Pears M Nisar I Houson J Blacker R Fieldhouse K Treacher	Prof S V Ley Prof A Holmes Dr C Ramarao R Gordon Dr Jin Yu C Mitchell	S Smith I Shirley	I McConvey A Wells D O'Beirne N Dealmeida J Hebblethwaite
		Millenium	
		D Tapolczay	

Microencapsulated Palladium(II) Products - Pd EnCat™

Product	Matrix Content %	Pd content mmol/g (%)	Co-encapsulated ligand	Average particle size micron
Pd(II) EnCat™ 40	40	0.4 (4)	-	150-200
Pd(II) EnCat™ 30	30	0.4 (4)	-	150-200
Pd(II) EnCat™ TPP30	30	0.4 (4)		150-200
Pd(II) EnCat™ TOTP30	30	0.4 (4)		150-200

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Microencapsulated Palladium Zero Nano Particulate Products

Product	Matrix Content %	Pd content mmol/g (%)	Co-encapsulated ligand	Average particle size micron
Pd(0) EnCat™ 40NP	40	0.4 (4)	-	150-200
Pd(0) EnCat™ 30NP	30	0.4 (4)	-	150-200

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