Biotage

User Group Meeting, 11th May 2006

Reaxa

Cleaner, Greener, Safer – Improving Precious Metal Catalytic Processes

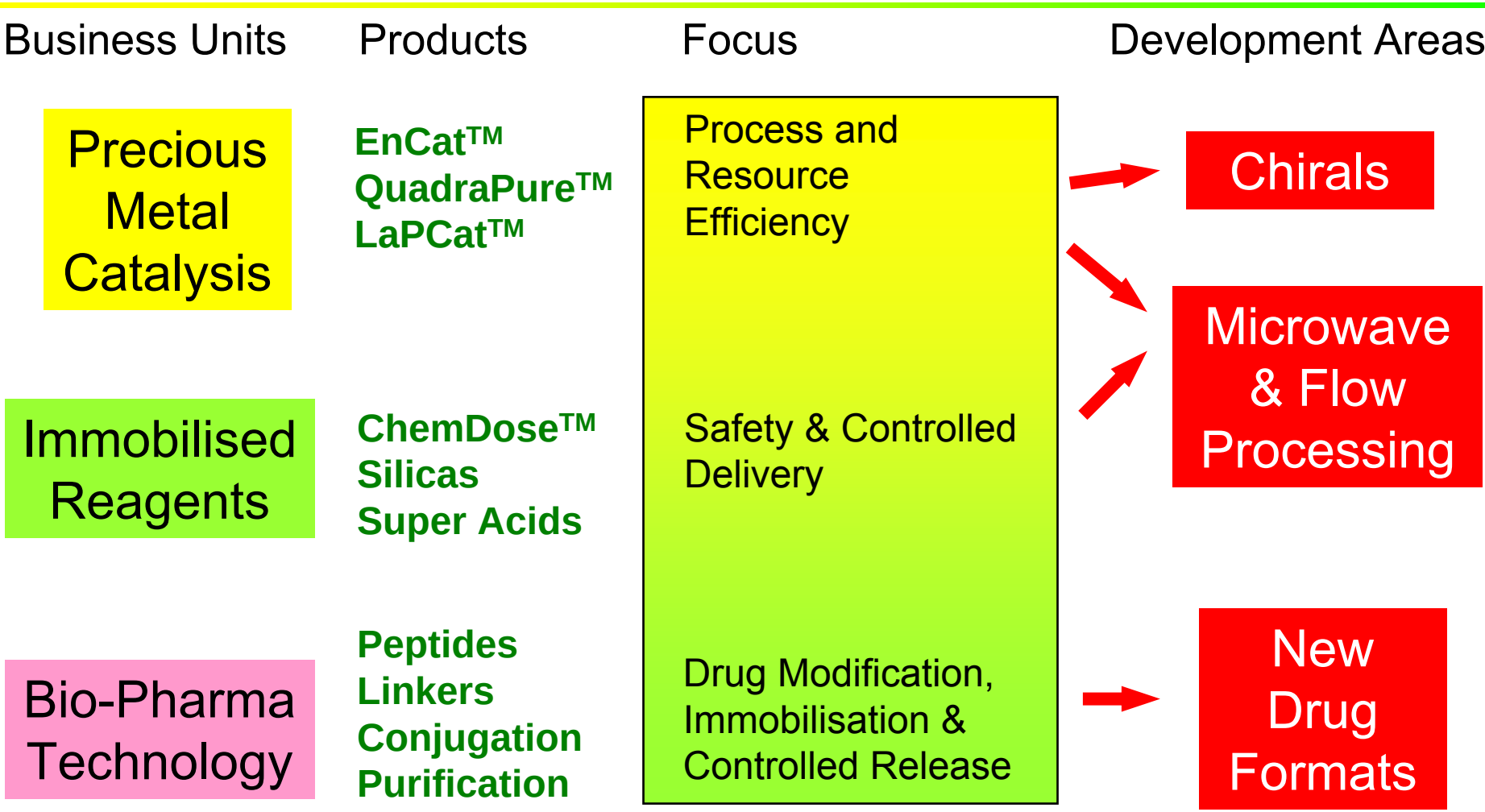
Clean Technologies for Precious Metal Chemistries

Reaxa

- spin-out from Avecia Pharmaceuticals
- collaboration with Professor Steve Ley and Dr Ian Baxendale at Cambridge University
- began trading in June 2005

Blackley, Manchester

Reaxa Technology



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'cleaner, greener, safer'

Microwaves at Reaxa

microwave heating is applied across all of Reaxa's technology platforms

Microwave

IAN R. BAXENDALE
MICHAEL R. PITTS

Microwave flow chemistry: the next evolutionary step in synthetic chemistry?

ABSTRACT

Microwave assisted chemistry is an increasingly important

routinely, safely and reproducibly carried out at a useful laboratory scale. Indeed, a significant proportion of medicinal lead candidates are currently prepared via a

Chemical Technology

Microwave-Enhanced Palladium-Catalysed Reactions

Microencapsulated palladium has been shown to be compatible with microwave heating, offering benefits such as increased yields, higher purities and simple work-up procedures, and permitting access to many previously unattainable molecular assemblies.

By Ian R Baxendale at the Department of Chemistry, University of Cambridge, and Mike Pitts at Reaxa Ltd

Dr Ian R Baxendale holds the Royal Society Wolfson Fellowship and is a Fellow of Sidney Sussex College, University of Cambridge. As the Director of New Technologies, he heads a new laboratory under the control of Professor Steven V Ley, aimed at process intensification and cleaner solutions to synthetic chemistry problems.

Dr Mike Pitts is Project Leader for microwave technology at Reaxa Ltd (Manchester, UK). Reaxa is a technology company addressing the chemical synthesis priorities of the life sciences and chemical industries – safety, cost-effectiveness and sustainability. The company grew from a partnership between industry and academia that set out in the mid-1990s to develop cleaner homogeneous catalysis: the programme was shared between Cambridge University, AstraZeneca, Syngenta and Avecia Pharmaceuticals. Following initial product launch at CPhI 2003, Reaxa was spun out of Avecia in mid-2005, and is now a combined venture between its management team, Cambridge University, Aveda and private investors. Dr Pitts's first degree was in Chemistry at Loughborough University, after which he completed a PhD with Professor Chris Moody at the University of Exeter, and a postdoctoral stay at the University of Vienna with Professor Johann Mulzer.

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Chemistry Today 2006, 24 (3) 42-45

Innovations In Pharmaceutical Technology 2005, (18), 86-90

Common Process Issues with Homogeneous Pd Catalysis

- Pd contamination of product – regulatory issue
- 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

minimise soluble Pd

downstream treatment

heterogeneous catalyst

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Why Use Precious Metal Scavengers in Pharmaceutical Manufacture?

- regulatory issue - stringent heavy metal limits set by FDA for APIs
- metal contaminants interfere with downstream chemistry
- economic work-up of PMG catalysed reactions is often over-looked until too late!
- the economic use of homogeneous PMG catalysts depends on ability to efficiently recover the PM
- to reduce waste stream pollution costs and killing water treatment plant
- prevention of reactor vessel M(0) contamination

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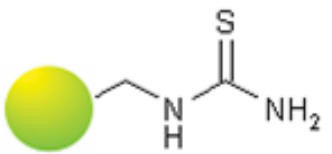
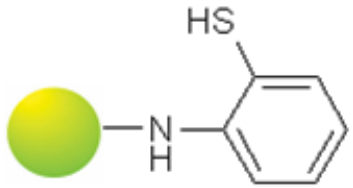
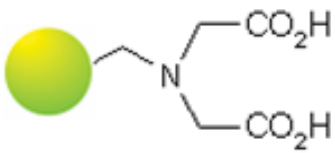
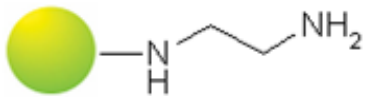
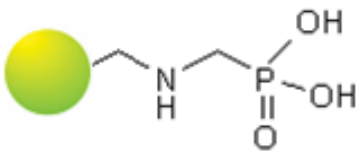
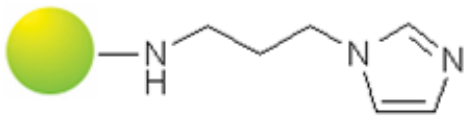
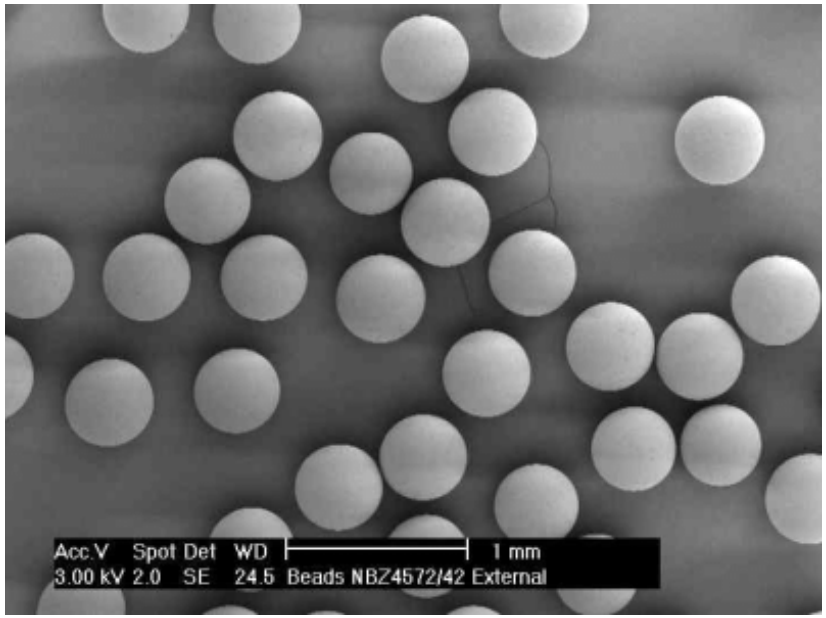
QuadraPure™ Products

QuadraPure™ Product *(macroporous resins)*		Aldrich catalogue #	QuadraPure™ Product *(microporous resins)*		Aldrich catalogue #
	TU	655422		MPA	657662
	IDA	657026		AEA	657646
	AMPA	657611		IMDAZ	657654

QuadraPure™ TU
Thiourea Macroporous Polystyrene



photograph of QuadraPure™ TU beads

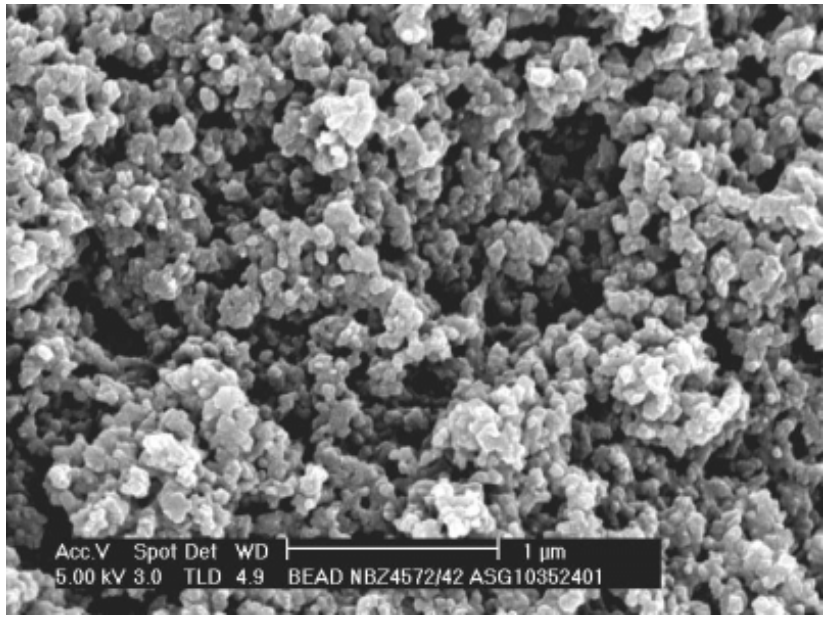
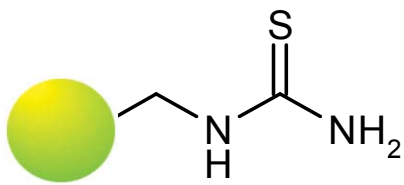


image of the interior of a QuadraPure™ TU bead



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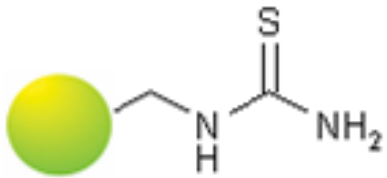
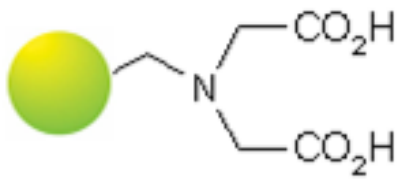
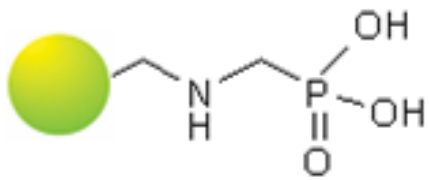
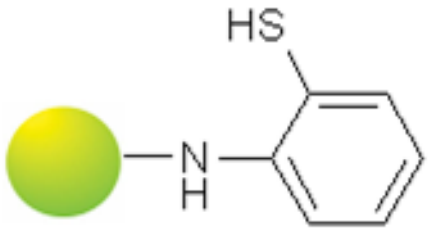
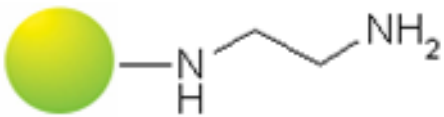
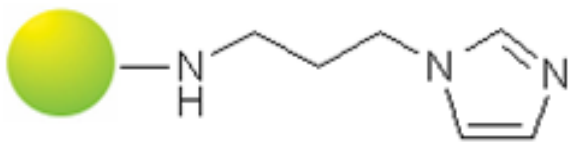
QuadraPure™ - Macroporous Products

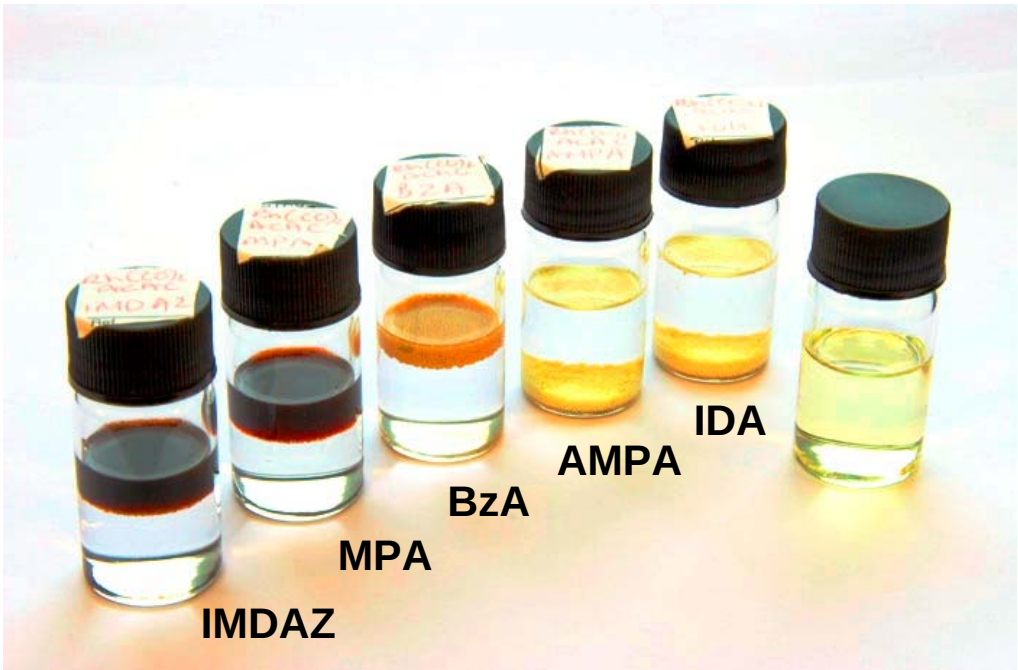
product	functional group	metals removed
 **QuadraPure™ TU**	thiourea	Pd, Pt, Ru, Au, Ag, Cu(I), Hg, Pb, Pt, Cd, Ni
 **QuadraPure™ IDA**	imino diacetate	Fe(II), Fe(III), Al(III), Ga(III), In(III), Cu, V, Pb, Ni, Zn, Cd, Be, Mn, Sr, Ba
 **QuadraPure™ AMPA**	aminomethyl phosphonic acid	Fe, Cu, Ni multivalent metal ions

Quadrapure™ - Microporous Products

product	functional group	metals removed
 **QuadraPure™ MPA**	mercaptophenyl amino	Pd, Ni, Cu, Sn and other soft transition metals
 **QuadraPure™ AEA**	aminoethyl amino	Pd and other transition metals
 **QuadraPure™ IMDAZ**	imidazol-1-yl propyl amino	Pd, Os, Co, Ni, V, Rh and other transition metals

QuadraPure™ Rh Scavenging

$Rh(CO)_2(acac)$



0.5 g resin for 1000 ppm solution in THF

$Rh(CO)(acac)PPh_3$ (hydroformylation catalyst)

QuadraPure™ MPA in THF

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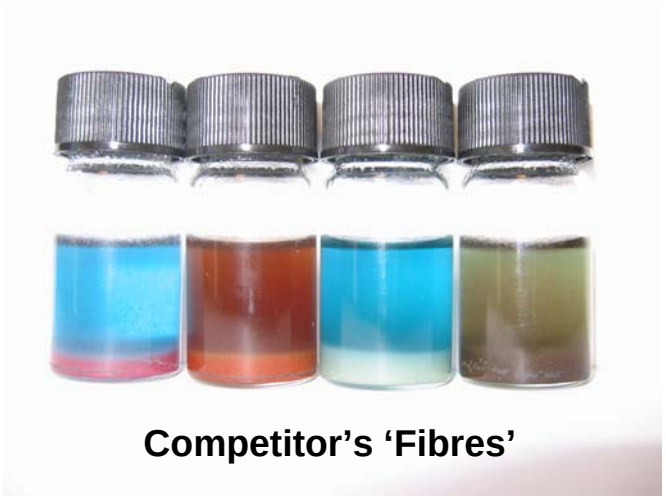
$[Rh(OAc)_2]_2$ /DMF Scavenger Trial

QUADRAPURE AEA, TU, BZA, EDA, DTC



Competitor's 'Fibres'

Competitor's 'Nets'

QuadraPure™

QuadraPure™

BzA

$[Rh(OAc)_2]_2$

DMF 1000 ppm

2-4 h at RT

microwave

10 min

80 °C

QuadraPure™

TU

$Pd(OAc)_2$

THF 1000 ppm

3-6 h at RT

microwave

10 min

100 °C

QuadraPure™

EDA

$Ni(acac)_2$

CH_2Cl_2 1000 ppm

48 h at RT

microwave

10 min

100 °C

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Resin Guide

QuadraPure™ Metal Scavenger Resins

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Volume of solution/ ml	Metal contamination level in solution (ppm)																
	10	25	50	100	200	300	400	500	600	700	800	900	1000	1500	2000	5000	10000
10	0.01	0.03	0.05	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1	1.5	2	5	10
25	0.03	0.06	0.13	0.25	0.5	0.75	1	1.25	1.5	1.75	2	2.25	2.5	3.75	5	12.5	25
50	0.05	0.13	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	7.5	10	25	50
75	0.08	0.19	0.38	0.75	1.5	2.25	3	3.75	4.5	5.25	6	6.75	7.5	11.3	15	37.5	75
100	0.1	0.25	0.5	1	2	3	4	5	6	7	8	9	10	15	20	50	100
200	0.2	0.5	1	2	4	6	8	10	12	14	16	18	20	30	40	100	200
300	0.3	0.75	1.5	3	6	9	12	15	18	21	24	27	30	45	60	150	300
400	0.4	1	2	4	8	12	16	20	24	28	32	36	40	60	80	200	400
500	0.5	1.25	2.5	5	10	15	20	25	30	35	40	45	50	75	100	250	500
750	0.75	1.88	3.75	7.5	15	22.5	30	37.5	45	52.5	60	67.5	75	113	150	375	750
1000	1	2.5	5	10	20	30	40	50	60	70	80	90	100	150	200	500	1000

Grammes of QuadraPure™ Required

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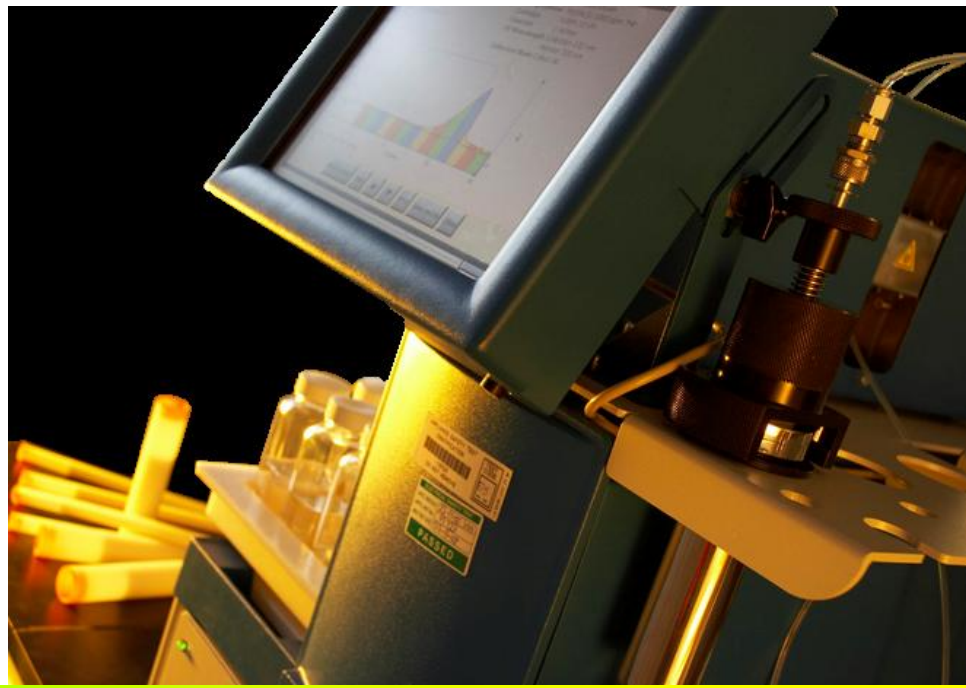
Scavenger Resins – Pharma Market Adoption Issues

historically metal scavengers seen as an R&D curiosity:

- too expensive for production
- not available at scale
- customers don't want to handle loose resin in reactors
- reactor validation issues

with Biotage, Reaxa are developing applications for the QuadraPure™ scavengers to overcome these issues



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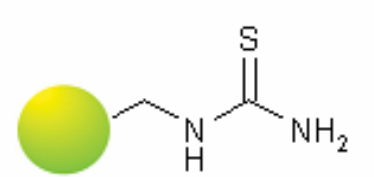
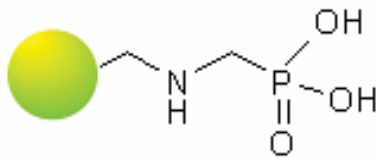
QuadraPure™ resins in cartridge format

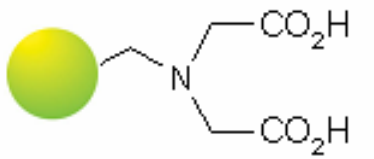
- TU, IDA, AMPA (+ BzA)
- launch sizes: 12M, 25S, 40M
  (6 g, 13 g, 68 g)



QuadraPure™ TU



QuadraPure™ AMPA



QuadraPure™ IDA

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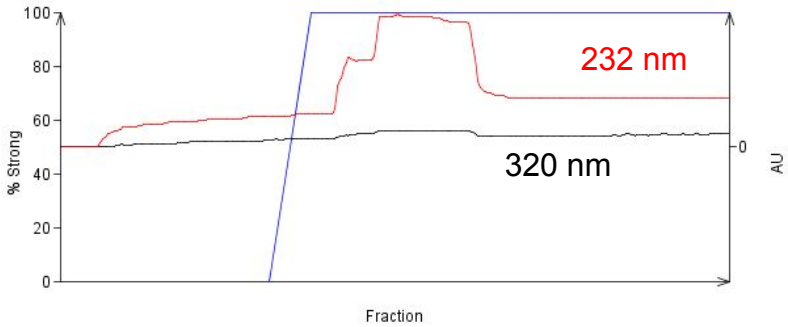
use in SP4 system

5 ppm Pd in THF
($Pd(OAc)_2$)



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QuadraPure™ TU cartridge: flow direction

Weak Solvent

tetrahydrofuran

Strong Solvent (blue line)

$Pd(OAc)_2$ 1000 ppm in THF

Cartridge

FLASH 12+M

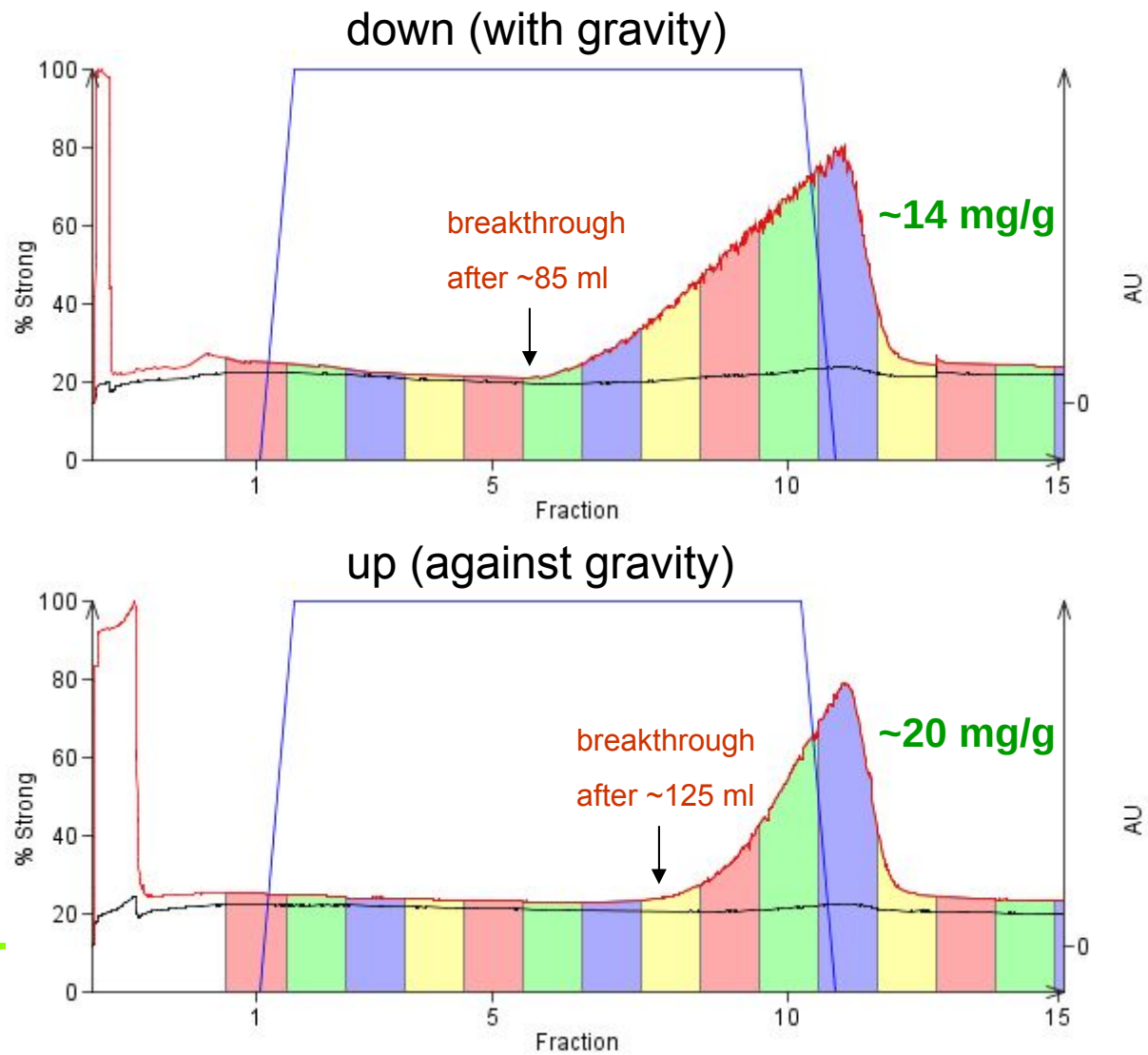
Flowrate

1 ml/min

UV Wavelength

Collection 232 nm (red line)

Monitor 320 nm (black line)



QuadraPure™ TU cartridge: flow direction

Weak Solvent

tetrahydrofuran

Strong Solvent (blue line)

$Pd(OAc)_2$ 1000 ppm in THF

Cartridge

FLASH 40+S

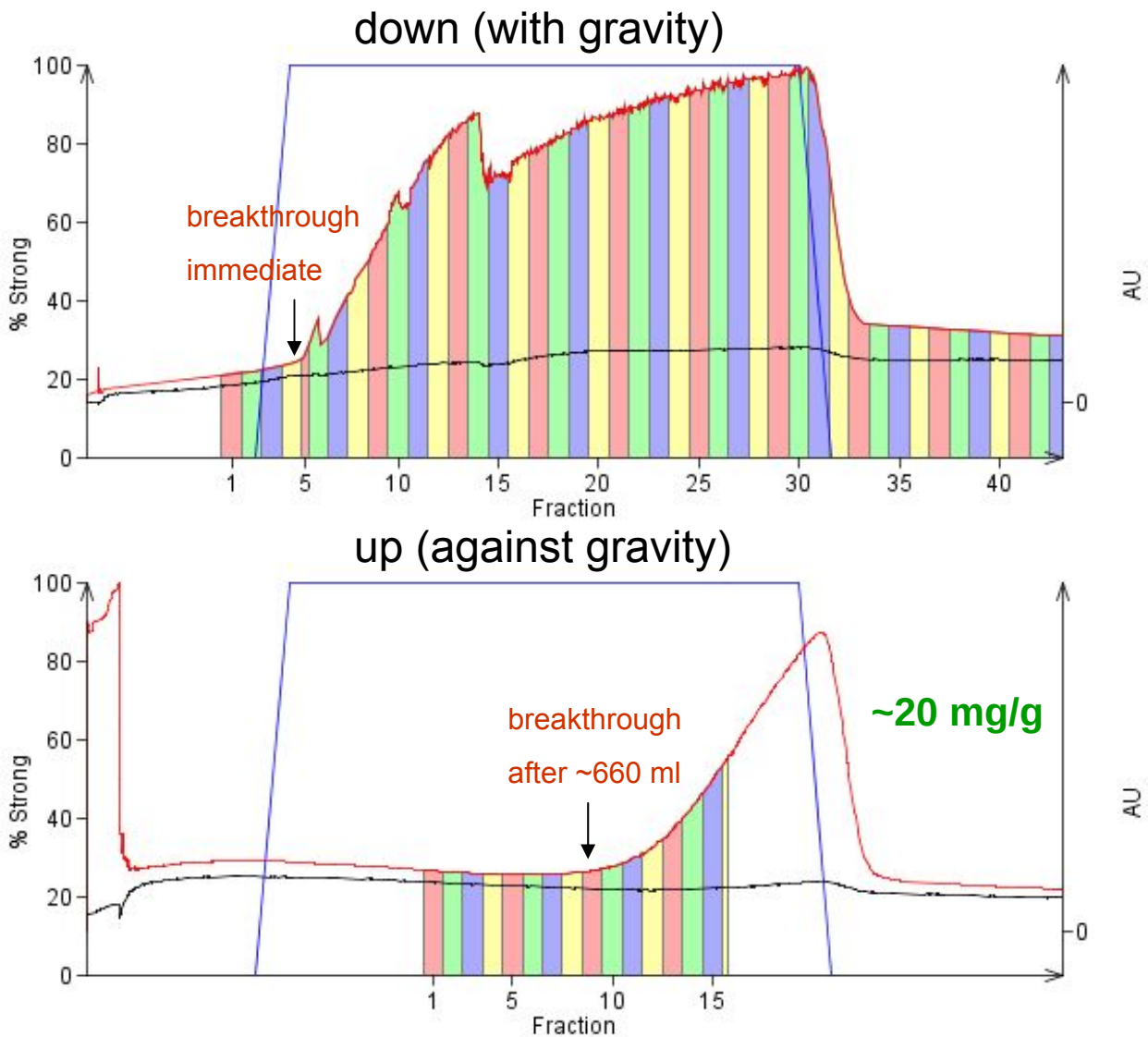
Flowrate

7 ml/min

UV Wavelength

Collection 232 nm (red line)

Monitor 320 nm (black line)



QuadraPure™ TU cartridge: 25S

Weak Solvent

tetrahydrofuran

Strong Solvent (blue line)

$Pd(OAc)_2$ 1000 ppm in THF

Cartridge

FLASH 25+S

Flowrate

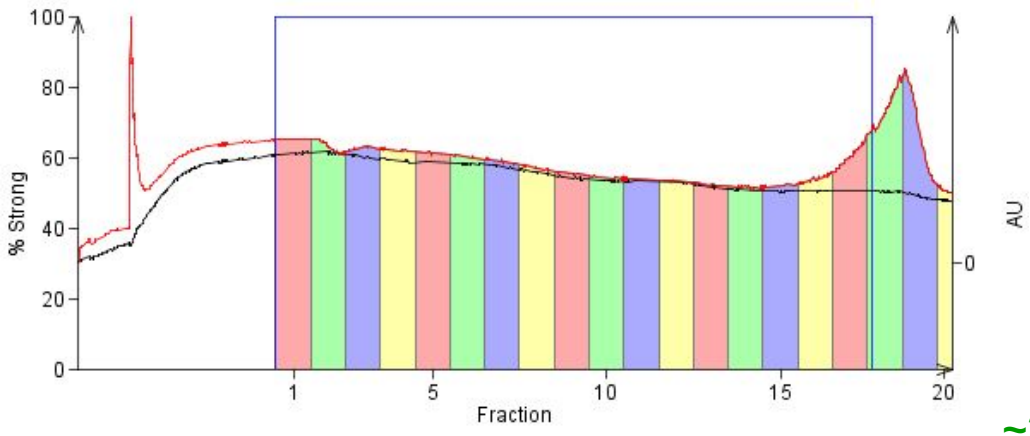
2 ml/min

UV Wavelength

Collection 232 nm (red line)

Monitor 320 nm (black line)

2 ml/min, 5 CV/h



~23 mg/g

2 ml/min, 5 CV/h - repeat

TU cartridges – $Pd(OAc)_2$ in THF

cartridge size			*flow rate*			*breakthrough*	
type	**vol. (ml)**	**mass QP (g)**	**up or down**	**(CV/h)**	**(ml/min)**	**(ml)**	**mg/g**
12M	12	6	down	6	1	85	14
12M	12	6	up	6	1	125	20
40S	66	34	down	6	7	10	-
40S	66	34	up	6	7	660	20
25S	24	13	up	5	2	300	23
25S	24	13	up	5	2 (repeat)	300	23
40M	132	68	up	~4	9	1300	19

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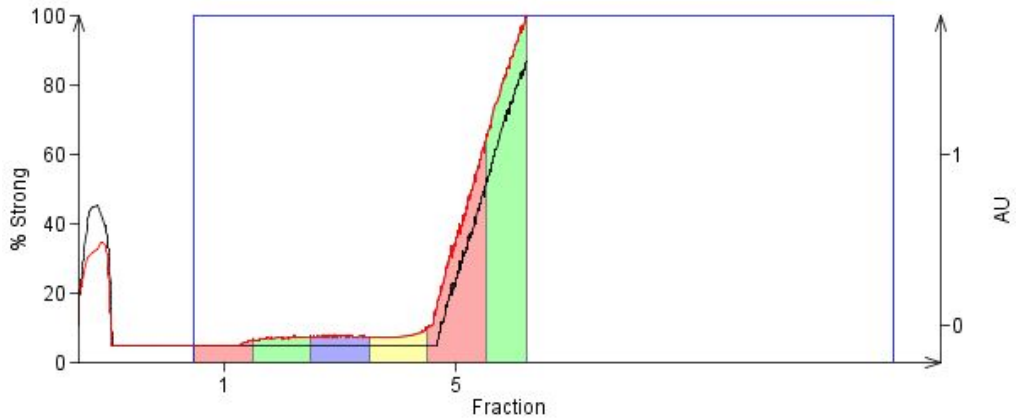
Initial Conclusions

- QuadraPure™ TU Fixed bed *vs.* Batch Capacity for Pd Removal is identical (Pd penetrates to near bottom of column)
- operating capacity is 20mg Pd/g resin
- flow rate determined by column bed volume which determines process time

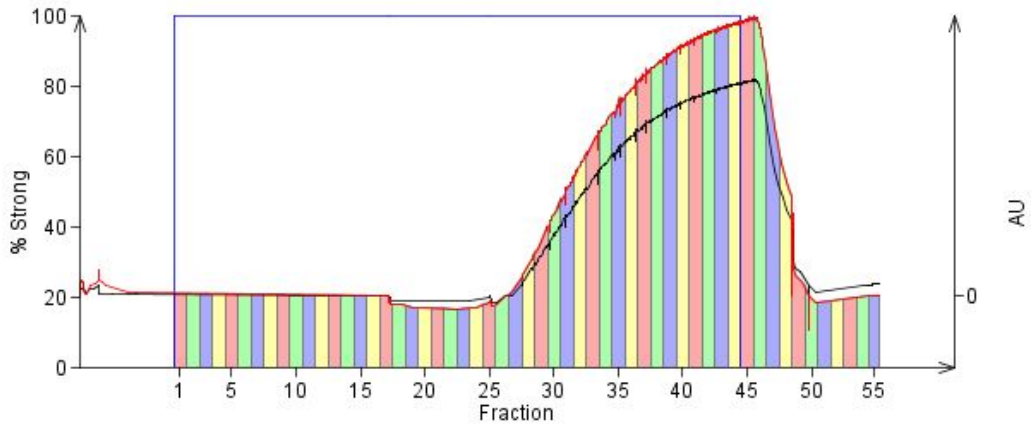
  optimum flow rates (with only integer pump values possible):
  - ***12M – at 1 ml/min***
  - ***25S – at 2 ml/min***
  - ***40M – at 8 ml/min***
- metal remains in cartridge once scavenged (cartridges flushed with 4 - 10 volumes of fresh solvent after breakthrough – no leaching of Pd)
- capacity is improved by flowing up *vs*. down (channelling issues)

QuadraPure™ cartridges

IDA cartridges – $Cu(acac)_2$ in DCM



AMPA cartridges – $FeCl_3$ in THF



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QuadraPure™ cartridges

IDA cartridges – $Cu(acac)_2$ in DCM ~0.3 mmol/g

cartridge size			*flow rate*			*breakthrough*	
type	**vol. (ml)**	**mass QP (g)**	**ppm**	**(CV/h)**	**(ml/min)**	**(ml)**	**mg/g**
12M	12	6	1000	5	1	120	20
25S	24	13	1000	5	2	300	23
40S	66	34	1000	4.5	5	700	21
40M	132	68	1000	4	8	1300	19

AMPA cartridges – $FeCl_3$ in THF ~0.2 mmol/g

cartridge size			*flow rate*			*breakthrough*	
type	**vol. (ml)**	**mass QP (g)**	**ppm**	**(CV/h)**	**(ml/min)**	**(ml)**	**mg/g**
12M	12	6	500	5	1	120	10
25S	24	13	500	5	2	400	15
40S	66	34	500	4.5	5	1100	15
40M	132	68	500	3	7	1400	10

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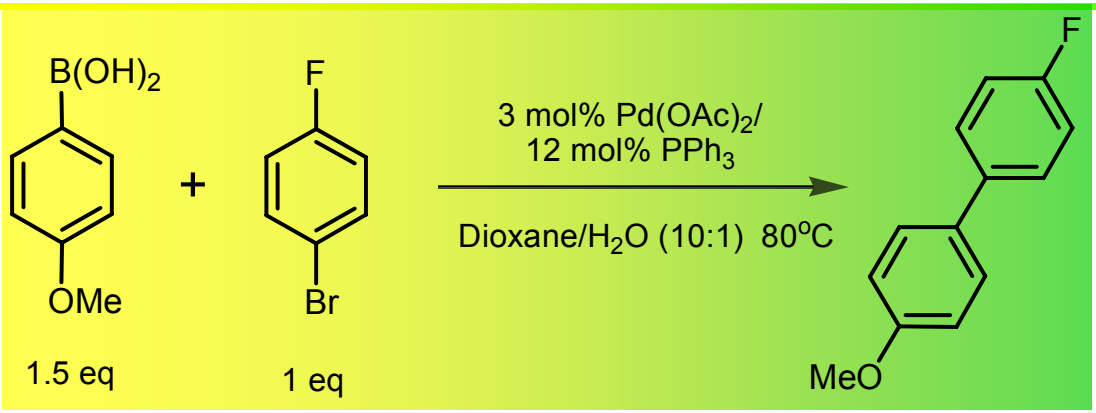
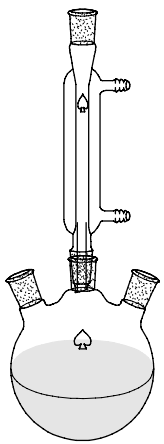
QuadraPure™ Pd process example

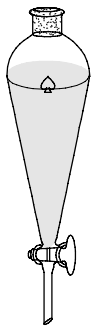
15 g scale

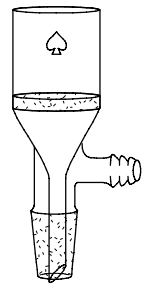
250 mg $Pd(OAc)_2$





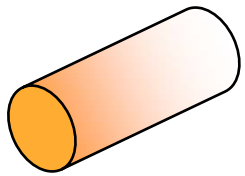
16000 ppm (3 mol%)





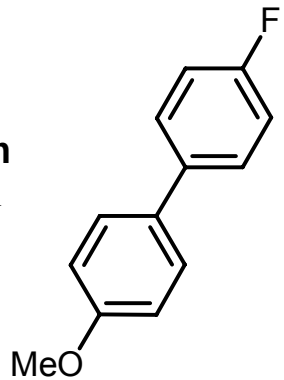
clarification (Celite™)

120 ppm



QuadraPure™ TU Flow cartridge

4 ppm



89% yield

QuadraPure™ TU cartridge delivers 97% Pd reduction

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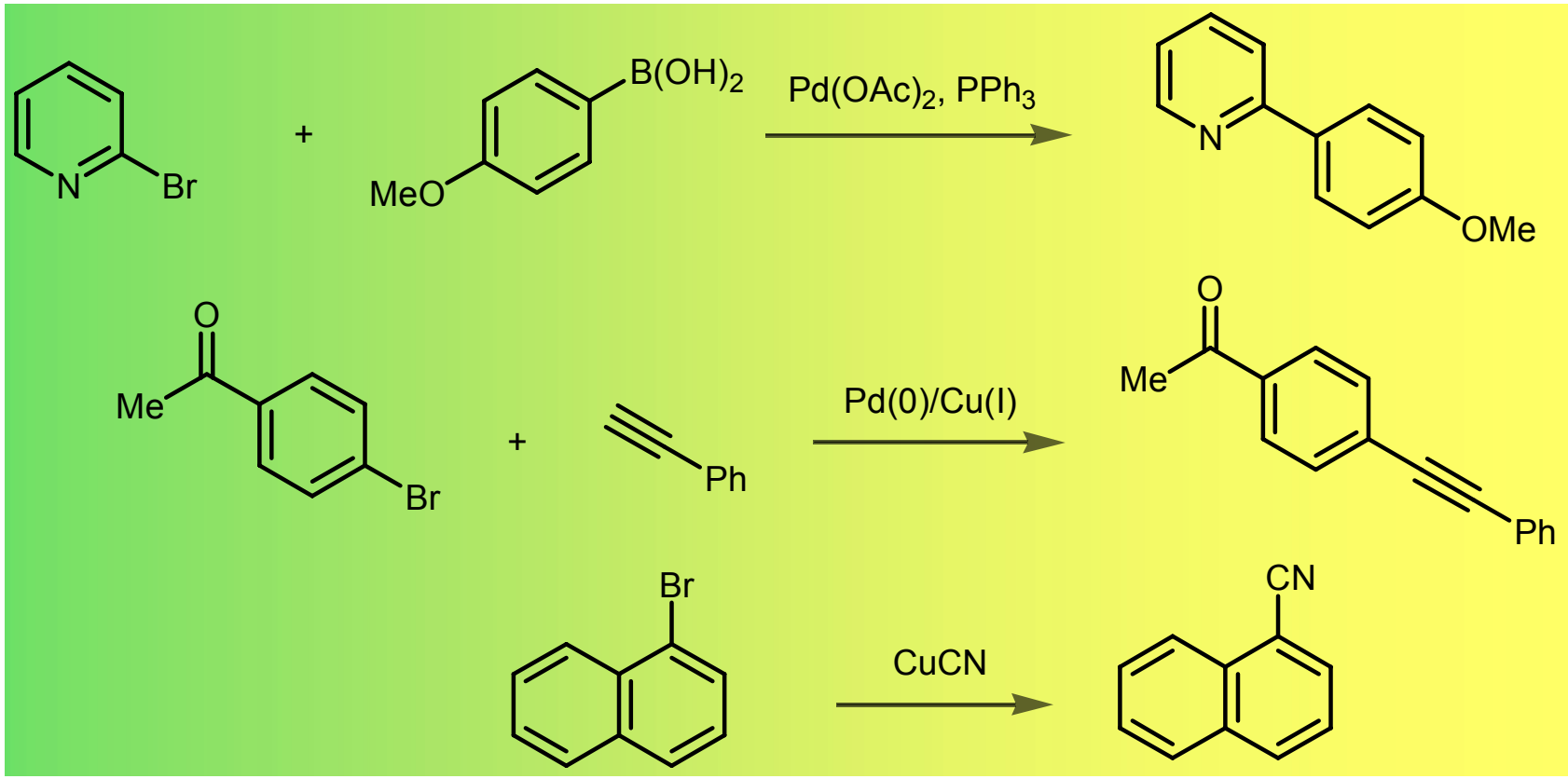
QuadraPure™ cartridges

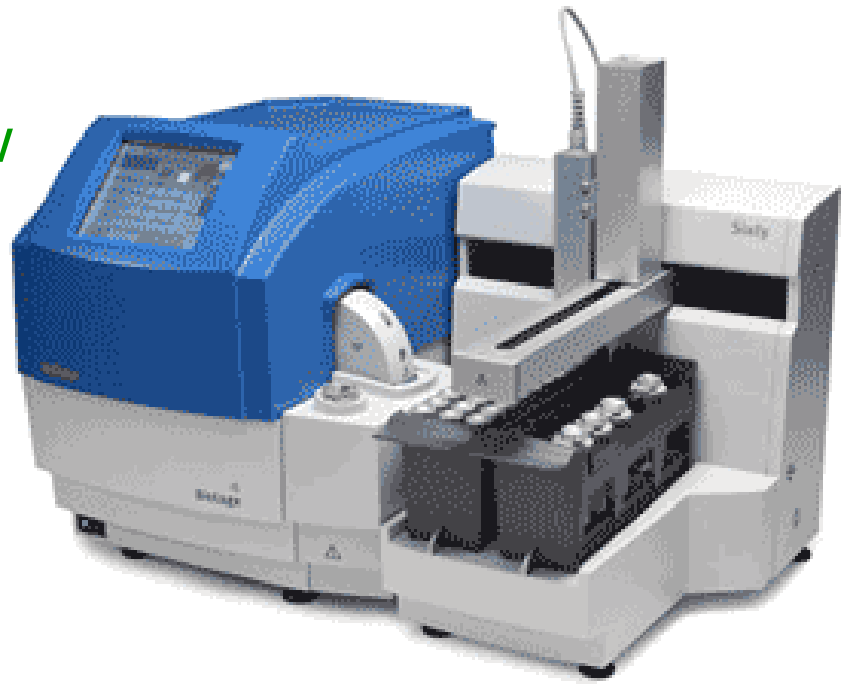
process representative, crude reaction outputs:



Microwave Technology

Microwave Development Work

- Designing range of Micro EnCat™ products specifically for use in microwave reactors
- Developing continuous-flow processes with EnCat™ technology

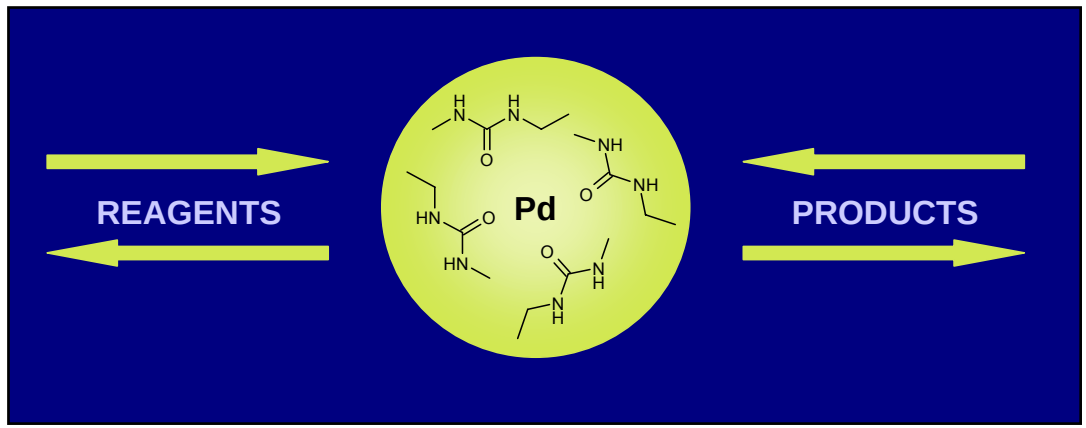


Reaxa

Microencapsulated Homogeneous Palladium Catalyst Technology

- excellent levels of activity in C-C bond forming reactions
- very low residual metal and ligand levels in product
- minimal waste stream contamination
- easy recovery of catalyst by filtration
- additional ligands not always required
- efficiency and economy gains through simple fast recovery and re-cycling
- mechanically and chemically robust
- high selectivity in transfer hydrogenation reactions

Pd EnCat™

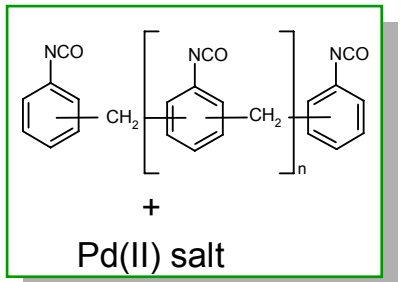


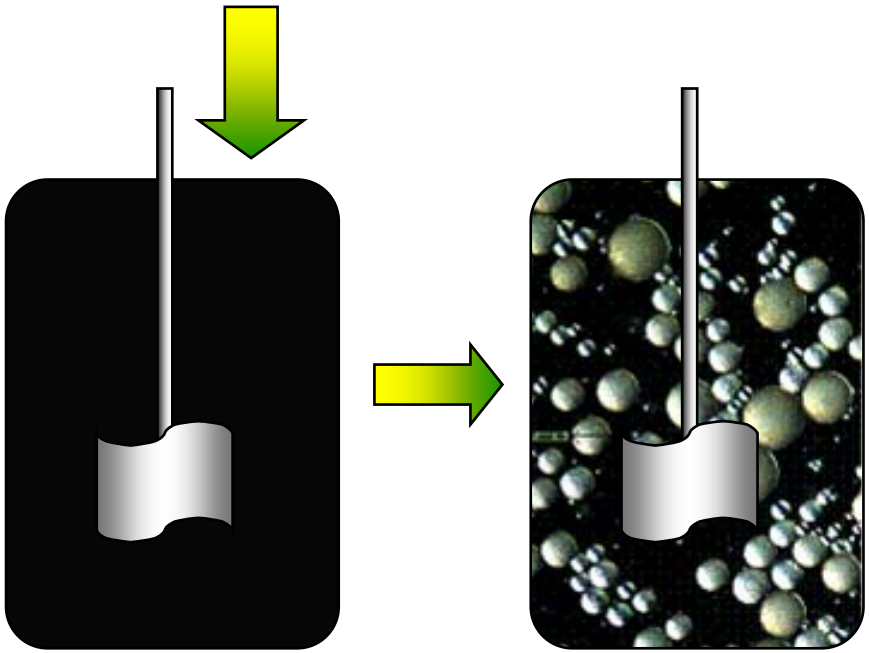
Reaxa

SIGMA-ALDRICH

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

Catalyst in organic solvent with cross-linking isocyanates





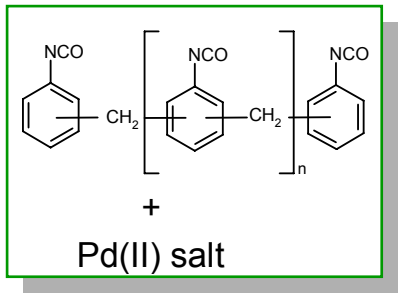
water, stabilisers

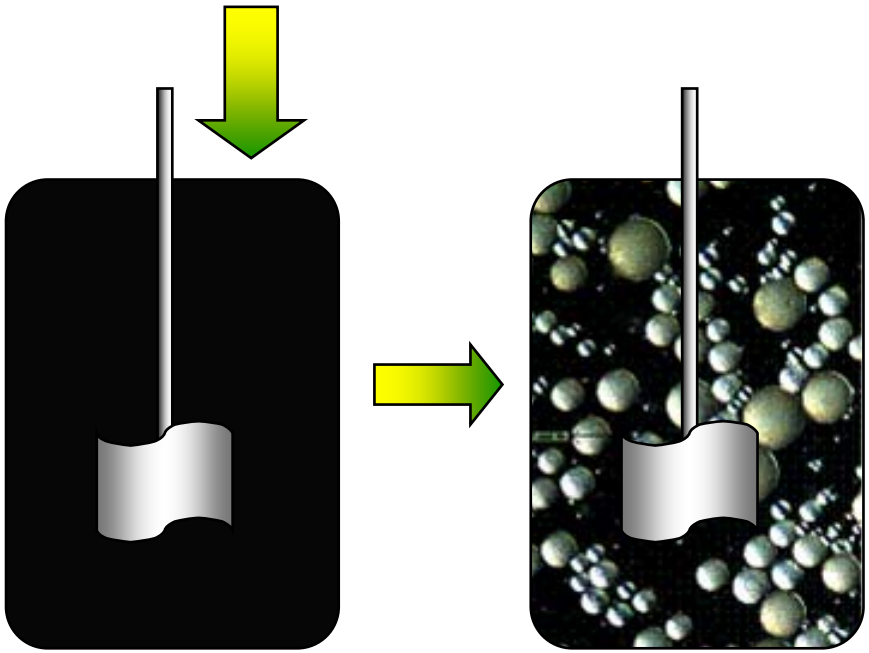
Oil-in-water emulsion

Reaxa

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

Catalyst in organic solvent with cross-linking isocyanates



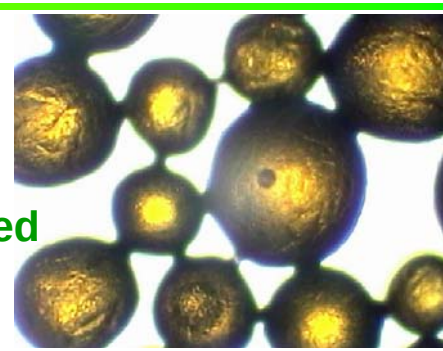


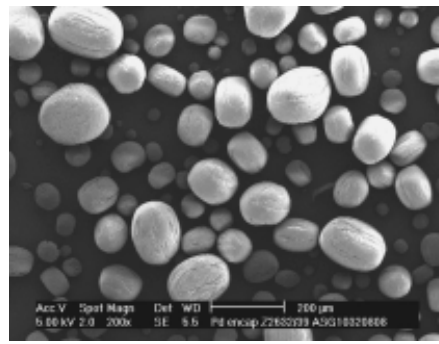
water, stabilisers

Oil-in-water emulsion

Heating initiates polymerisation

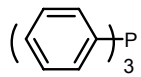
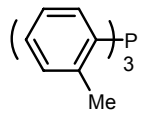
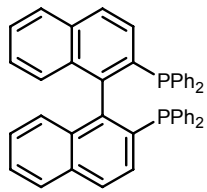
Filtered & dried EnCat™ 50-300μm



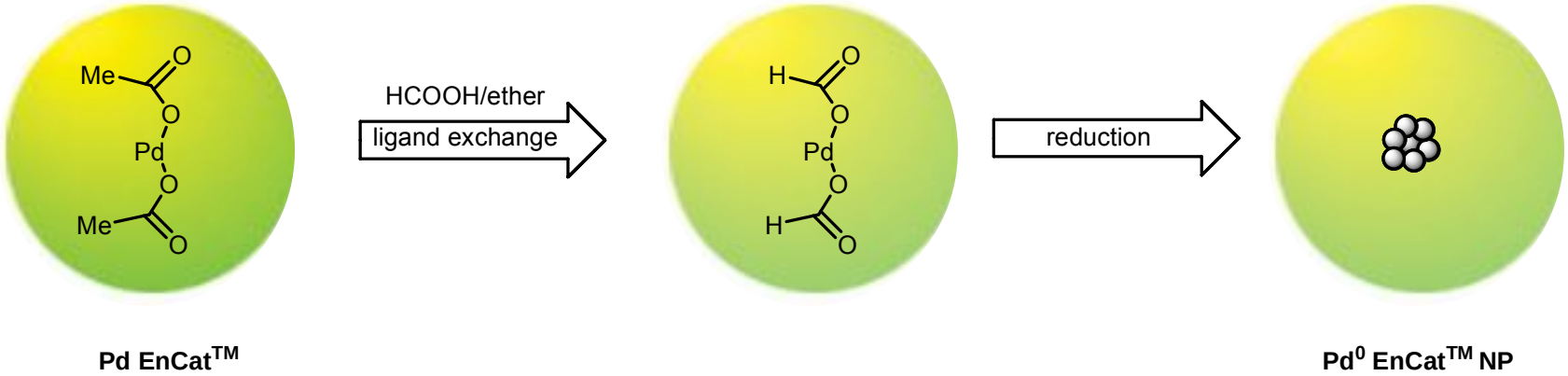


Reaxa

Pd EnCat™ Products

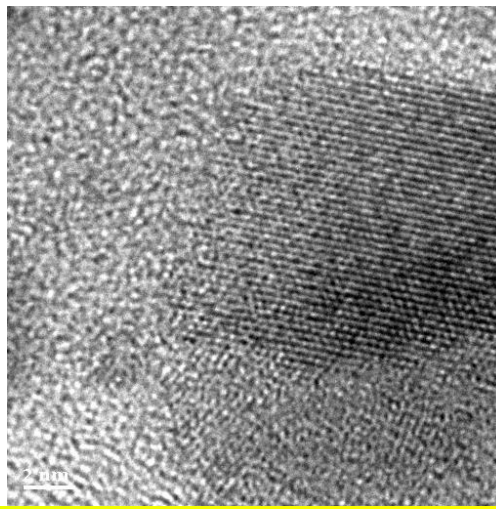
product	*Aldrich cat. no.*	*Pd content %w/w*	*co-encapsulated ligand*
Pd(II) EnCat™ 30	644714	4.3	none
Pd(II) EnCat™ 40	644722	4.6	none
Pd(II) EnCat™ TPP 30	644706	4.7	
Pd(II) EnCat™ TOTP 30	644692	4.7	
Pd(II) EnCat™ BINAP 30	658693	4.7	
Pd(0) EnCat™ 30 NP	653667	4.3	none

Pd(0) EnCat™ NP30



Pd EnCat™ **Pd^0 EnCat™ NP**

- **Pd particles <2 nm (approx 10 atoms)**
- **Nanostructure stabilised by polyurea matrix**
- **Highly active and recyclable H_2 transfer catalyst**
- **High chemoselectivity**
- **Non pyrophoric - easy and safe to handle *vs.* Pd/C**
- **Very low metal contamination of product**
- **Easy recovery and recycle of catalyst from process vessel**



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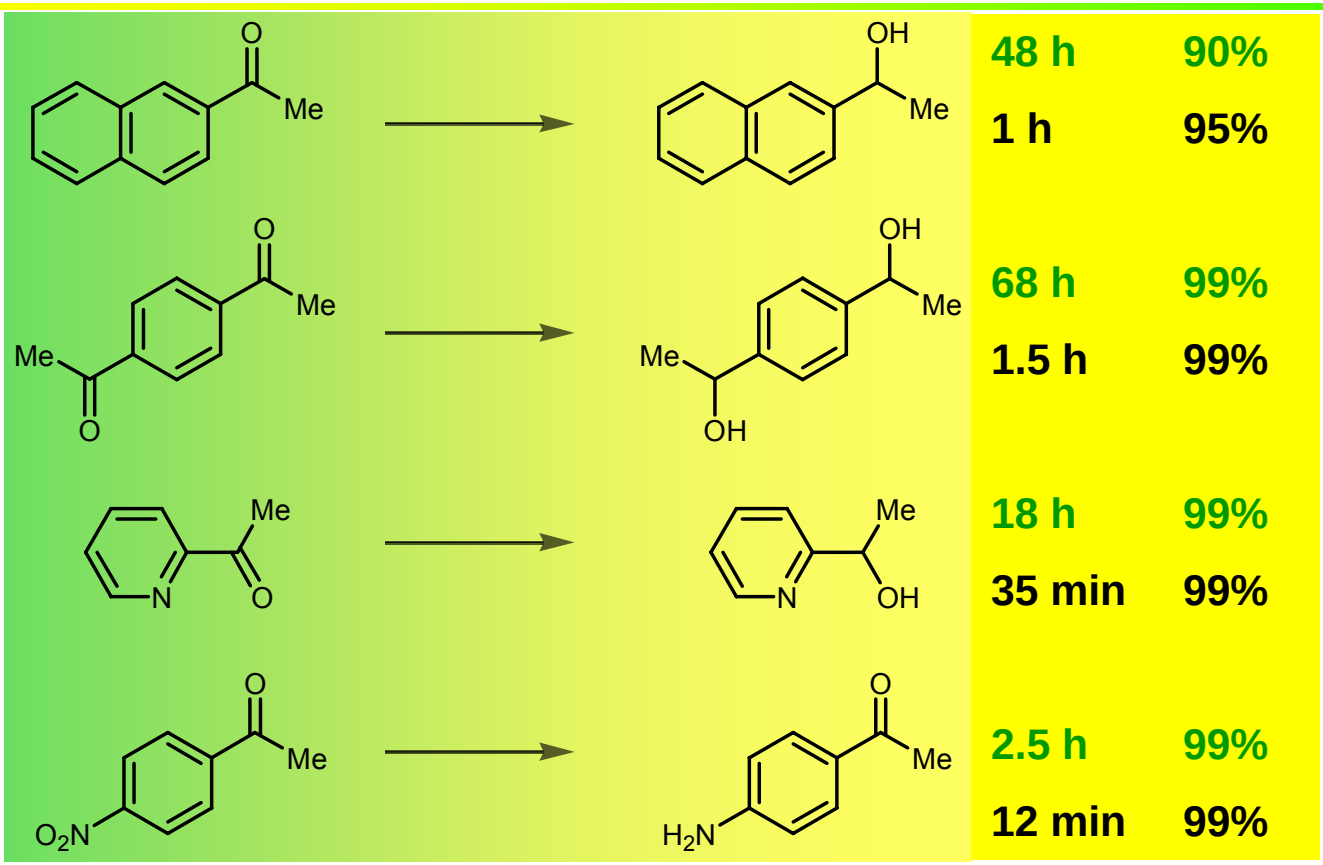
Pd(0) EnCat™ NP30



EtOAc, Et_3N (20 eq), HCOOH (20 eq), Pd(0) EnCat NP, rt

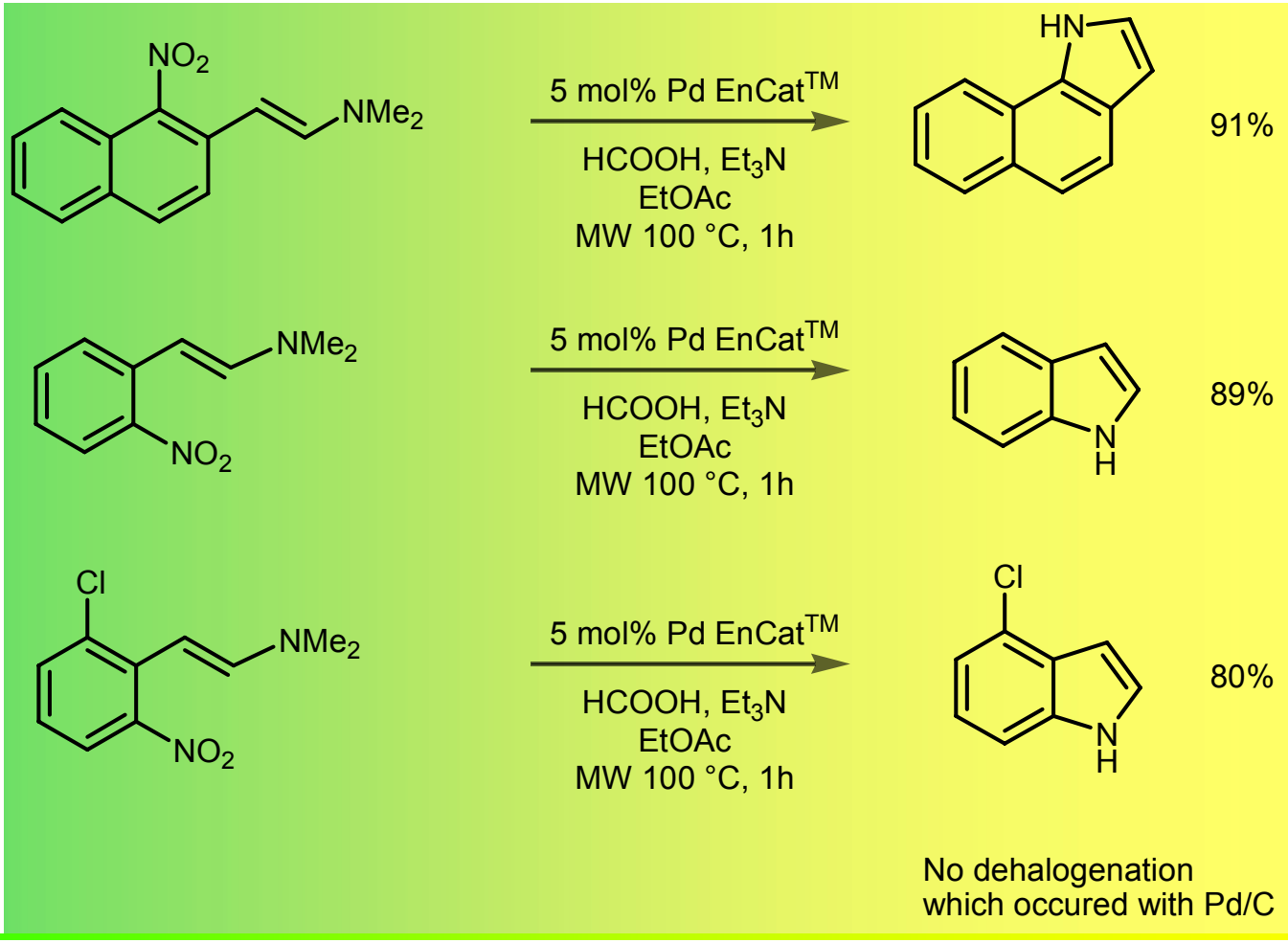
EtOAc, Et_3N (5 eq), HCOOH (5 eq), Pd(0) EnCat NP, MW 120 °C

Reaxa

SV Ley et al Chem Comm 2003, 678

Pd(0) EnCat™ NP30

Leimgruber-Batcho

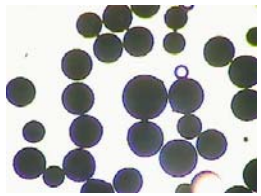


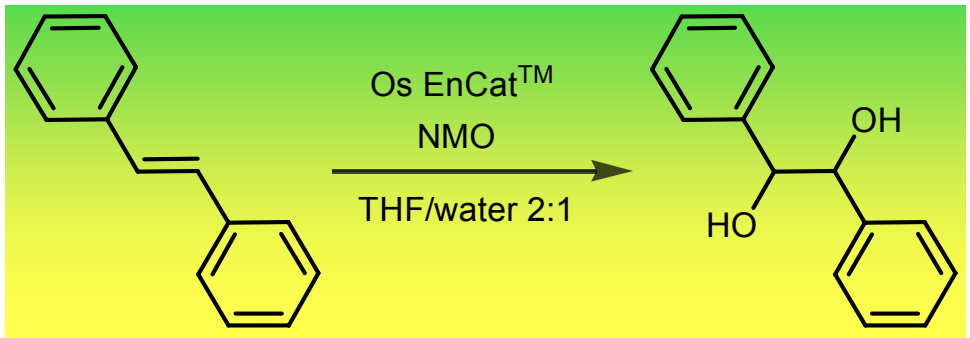
Reaxa

SV Ley *et al Org. Biomol. Chem.* 2004, 2, 160-167

Microencapsulated Osmium Tetroxide

Os EnCat™



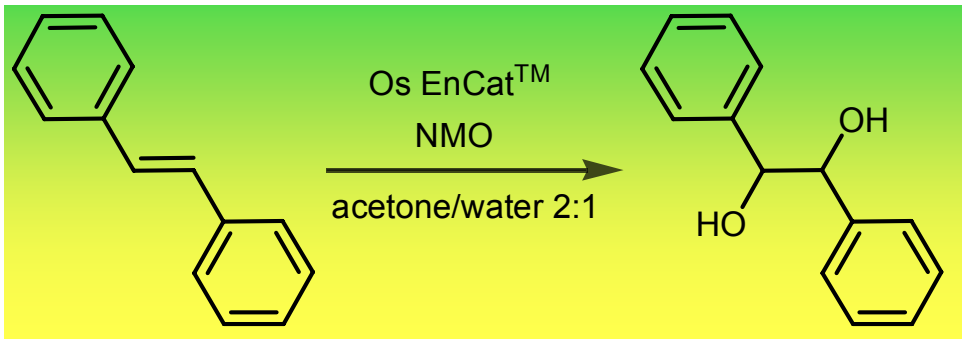


Temp °C	Yield %	Os ppm
20	0	30
40	100	-
60	100	120

Reaxa

SIGMA-ALDRICH

Microencapsulated Osmium Tetroxide



MW 80 °C, 20 min

91%

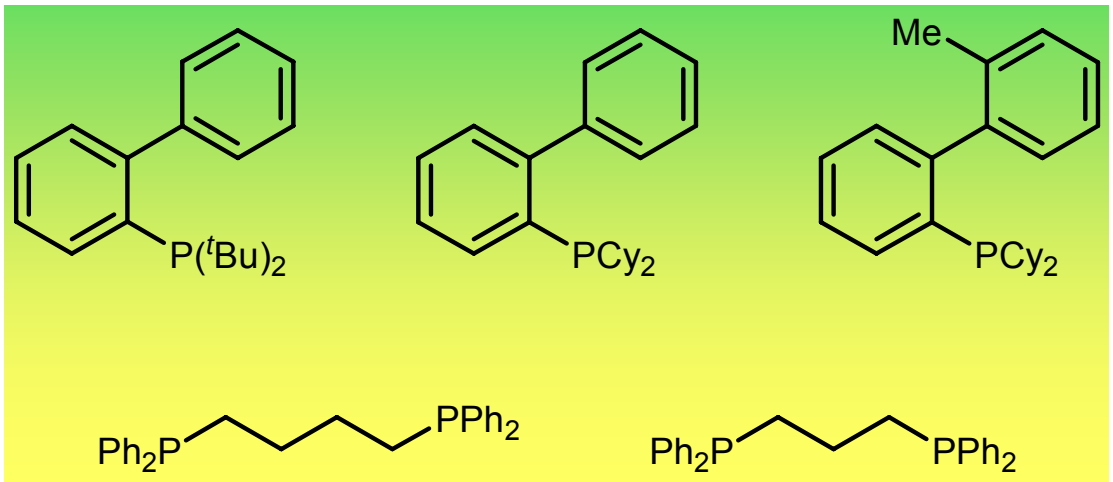
Os EnCat™

Reaxa

development EnCat™

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

- **metal type and loading**
- **ligand type and loading**
- **matrix porosity and particle size**

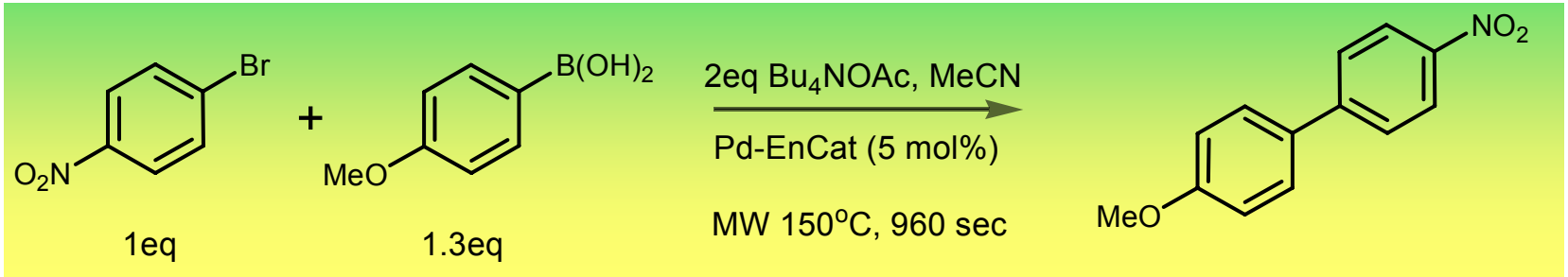


In development:

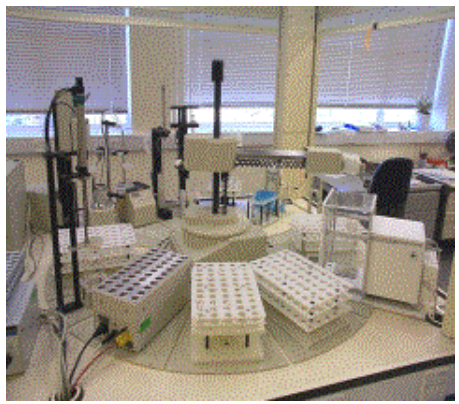
- **nickel**
- **platinum**
- **chirals**
- **your catalyst…?**
- **Micro EnCat™**

Reaxa

Pd(II) EnCat – Suzuki Chemistry



Microwave Synthesis

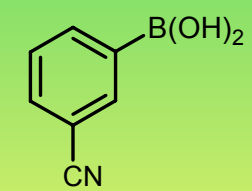


Filtration & evaporation

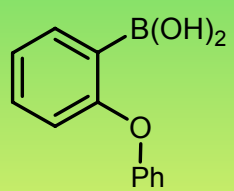
Purification (Bond Elut) & analysis

Analysis of Results

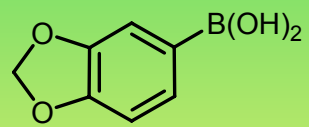
- **Matrix of 12 boronics x 19 heteroaromatic bromides to give 228 possible products**
- **157 products isolated (68% success rate) – no single reaction optimised Average Yield = 37% after purification (range 1% - 75%)**



13/19



10/19



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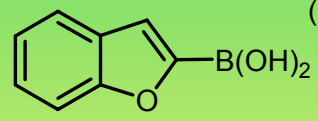

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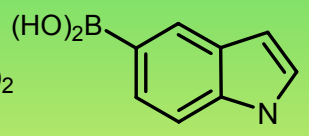

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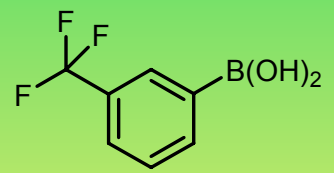

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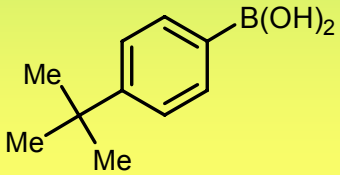

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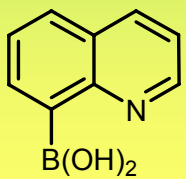

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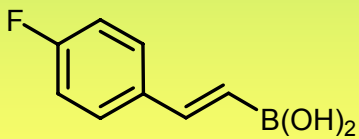

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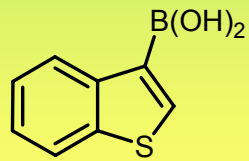

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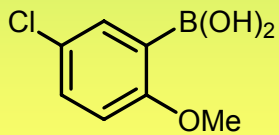

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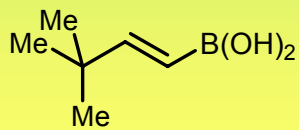
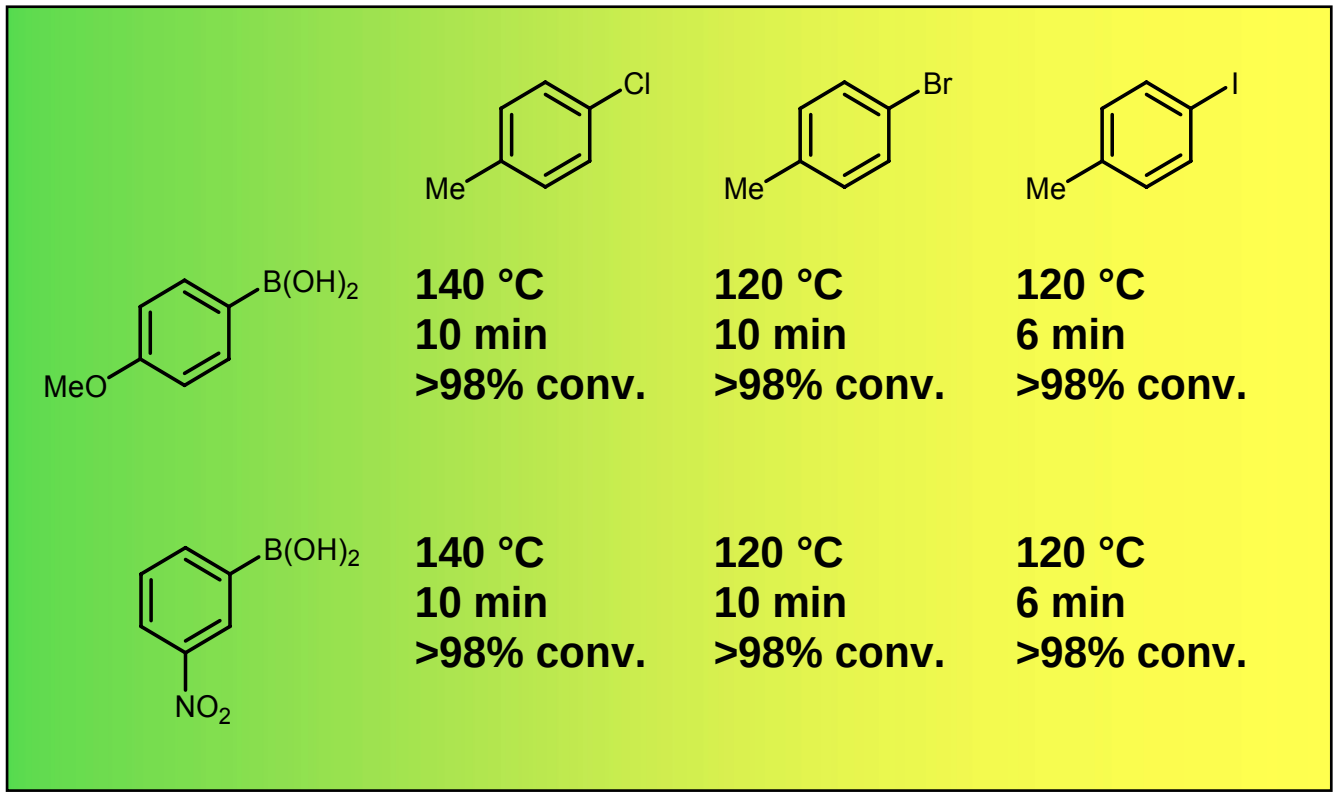


16/19

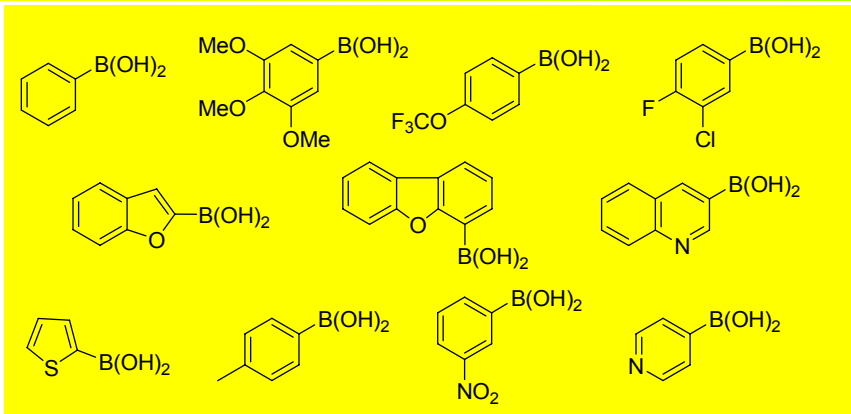
Pd(II) EnCat – Suzuki Chemistry

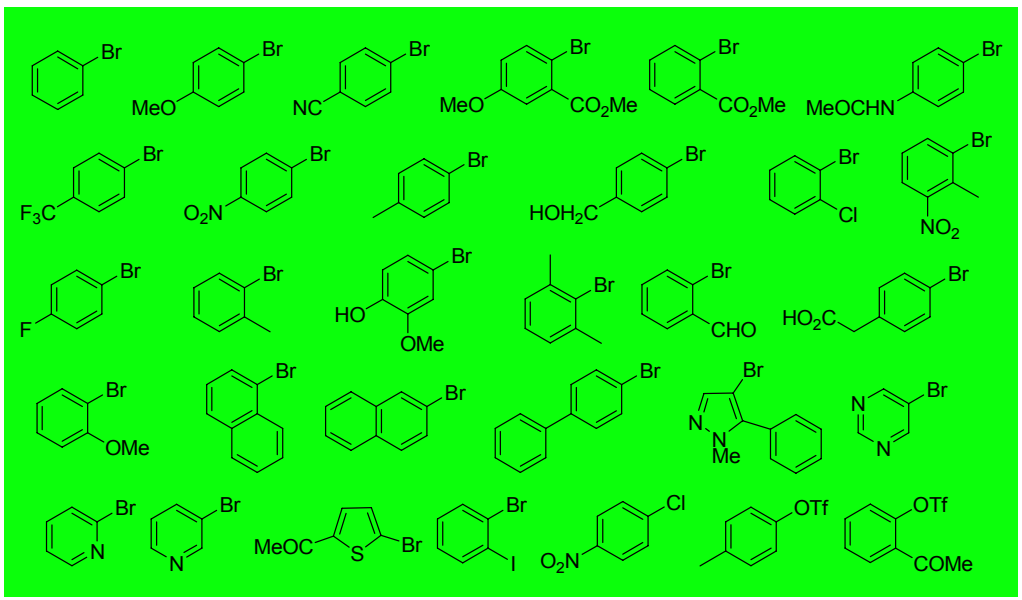
Optimised conditions



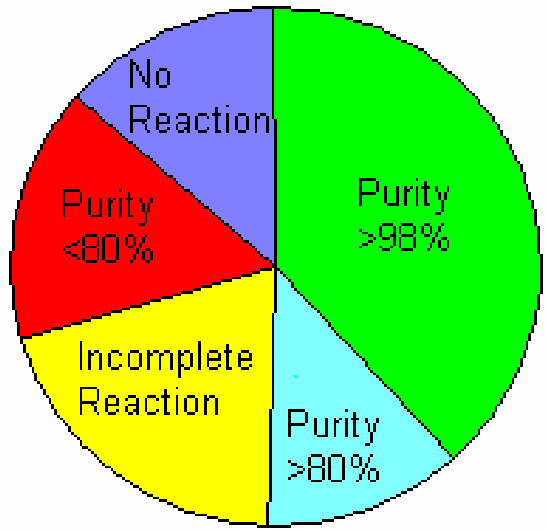
0.5 mmol halide, 0.5 mmol boronic acid, 1.0 mmol Bu_4NOAc, 0.025 mmol Pd EnCat™, EtOH, microwave irradiation

Pd(II) EnCat – Suzuki Chemistry





374 reaction library

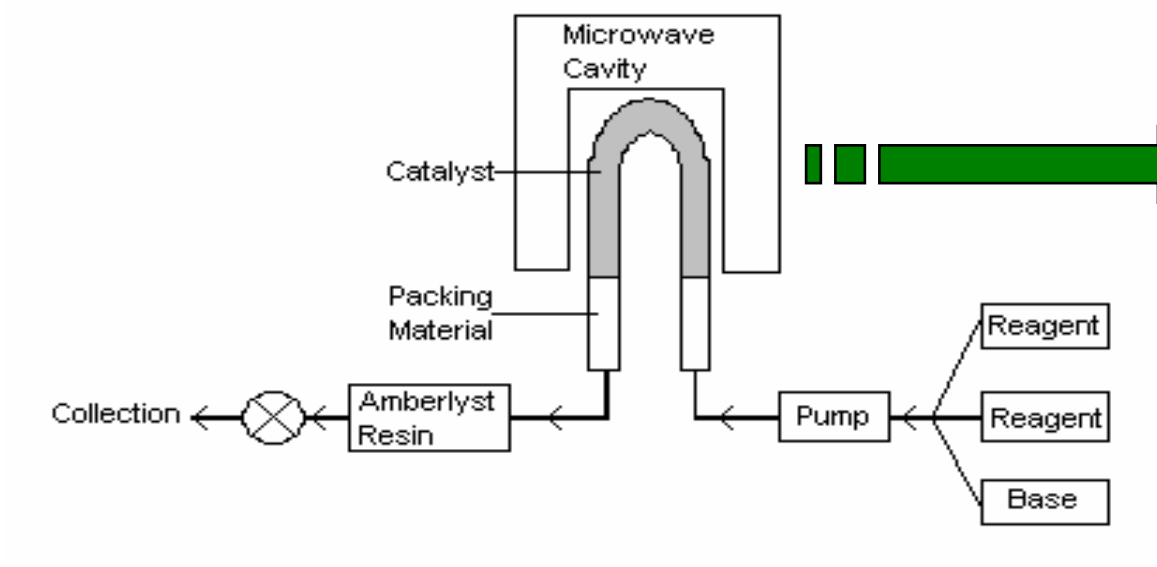


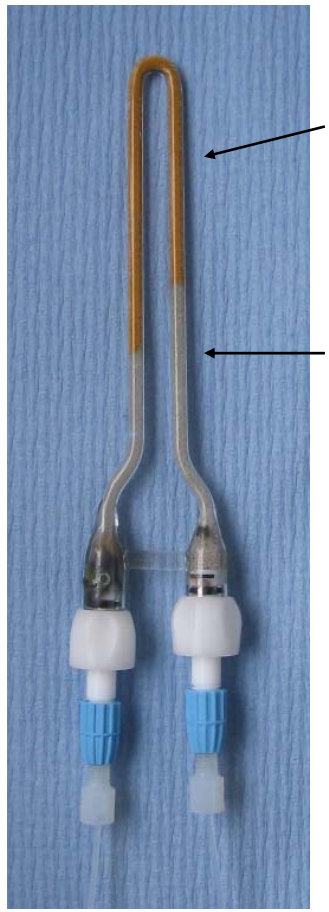
193

>80% yield

>90% purity

continuous-flow microwave reactor



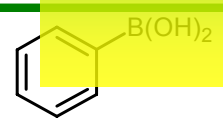
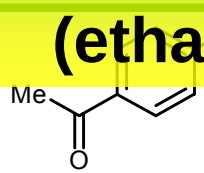
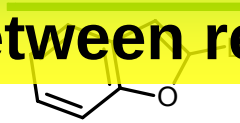
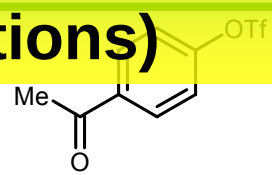
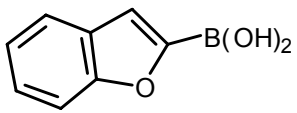
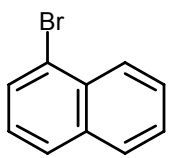
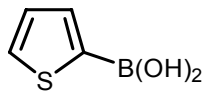
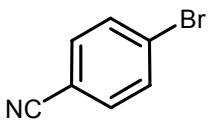
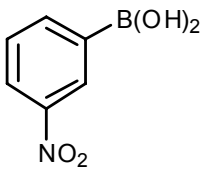
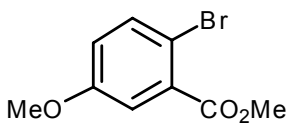
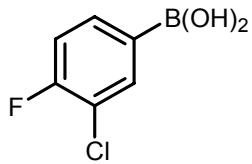
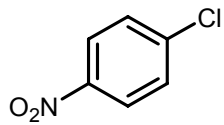
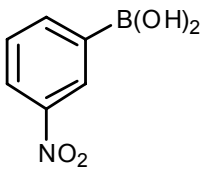
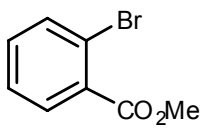
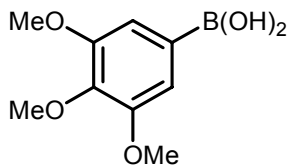
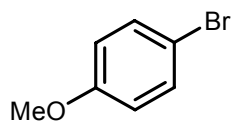
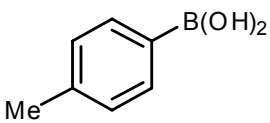
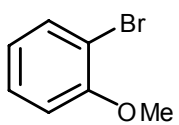
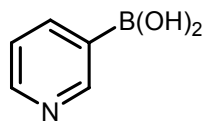
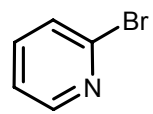


- heating cycles: 50 W for 30 s then cooling 18 s
- 0.1 ml/min flow rate, 0.01 – 0.07 M reagent mix
- 40 bar back flow regulator
- product obtained without need for purification

continuous-flow *vs* batch

performed sequentially over the same catalyst bed

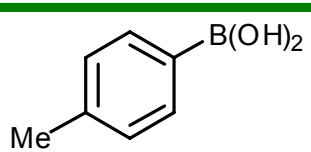
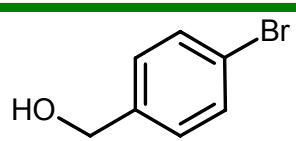
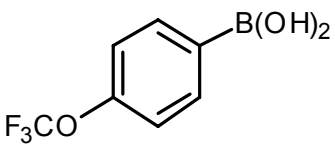
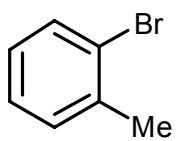
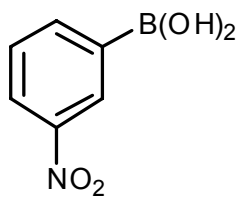
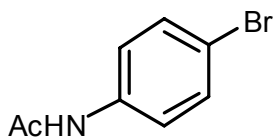
(ethanol wash between reactions)

boronic acid	halide	batch	flow	boronic acid	halide	batch	flow
						purity	
						30%	91%
		82%	>98%			26%	>98%
		64%	>98%			23%	>98%
		54%	92%			16%	91%
		40%	94%			5%	82%

Reaxa

little variation in yield between methods generally ~90%

continuous-flow: improved purity

boronic acid	halide	purity		
		batch	batch + cooling	flow
		42%	86%	>98%
		48%	>98%	>98%
		32%	96%	>98%

flow rate 0.1 ml/min; pulsed heating at 50 W for 30 s then 18 s cooling

0.5 mmol halide, 0.5 mmol boronic acid, 1.0 mmol Bu_4NOAc, 0.025 mmol Pd EnCat™, EtOH, microwave irradiation
purity measured by LCMS and ^1H NMR.

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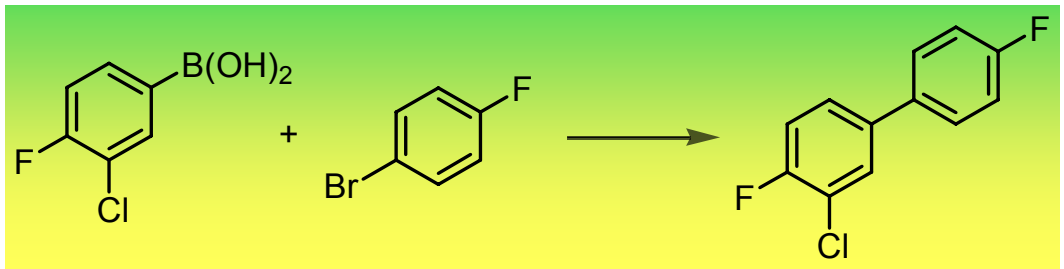
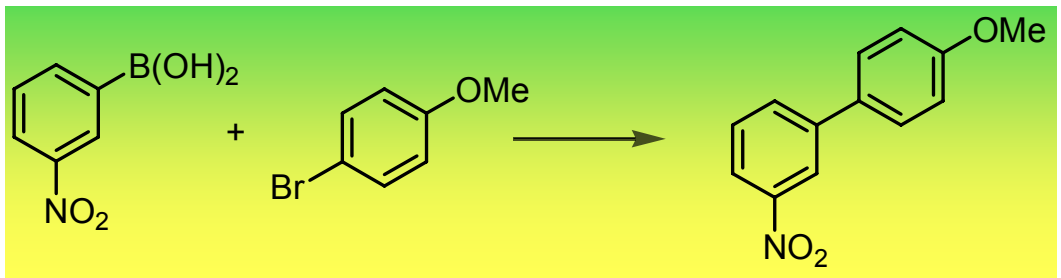
continuous-flow microwave reactor

- flow reactor run continuously and conversion monitored
- catalyst loading corresponds to ~0.2 mol%



172 mg Pd EnCat™
28 h
7.53 g product



182 mg Pd EnCat™
34 h
9.34 g product

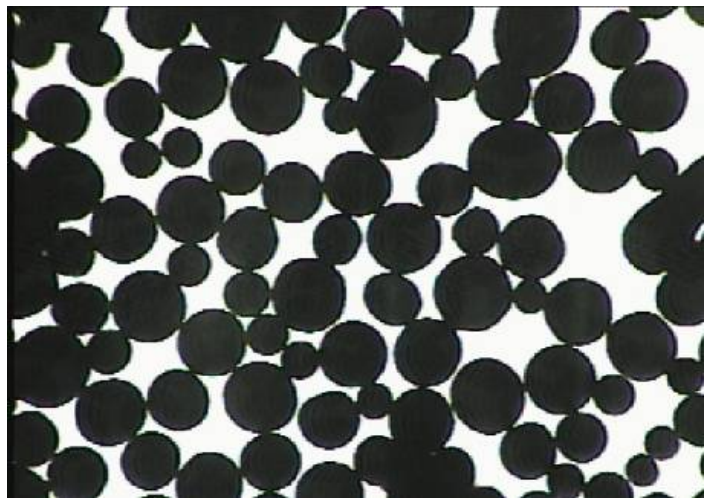
1 eq. halide, 1 eq. boronic acid, 2 eq. Bu_4NOAc, 0.2 M in EtOH
Pd EnCat™, microwave irradiation; flow rate 0.2 ml/min

Approaches to Micro EnCat

Requirements:

- Low levels of Pd and P contamination - < 5 ppm and < 20 ppm
- Ease of handling and recovery of catalyst
- Use in fixed bed/flow systems

- Enhanced matrix stability
  - Increased crosslink density
  - Alternative isocyanates (possibly mixed)
- Enhanced metal binding
  - Modification of matrix
  - Several approaches considered



polyTPP Pd EnCat

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Pd EnCat™ 30, palladium acetate,
microencapsulated in polyurea
matrix, 0.4 mmol Pd/g
International patent application PCT/GB 02/03135

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Micro EnCat™

	Micro EnCat	Pd EnCat TPP30	Pd EnCat 30
Incorp. Of Pd $(OAc)_2$/%	99	97	80
Incorp. Of P ligand/ %	99	96	-

Pd content	**4.3-4.9 w/w%**
Pd loading	**0.40-0.46 mmol/g**
P loading	**0.18-0.22 mmol/g**
particle size	**50-310 μm (185 av.)**

- Efficient encapsulation of Pd and phosphine metal (low losses)
- Excellent catalytic activity in standard Suzuki reaction
- Lower levels of Pd contamination in crude product than other P catalyst
- Bound-in metal demonstrated by low Pd levels in treated catalyst

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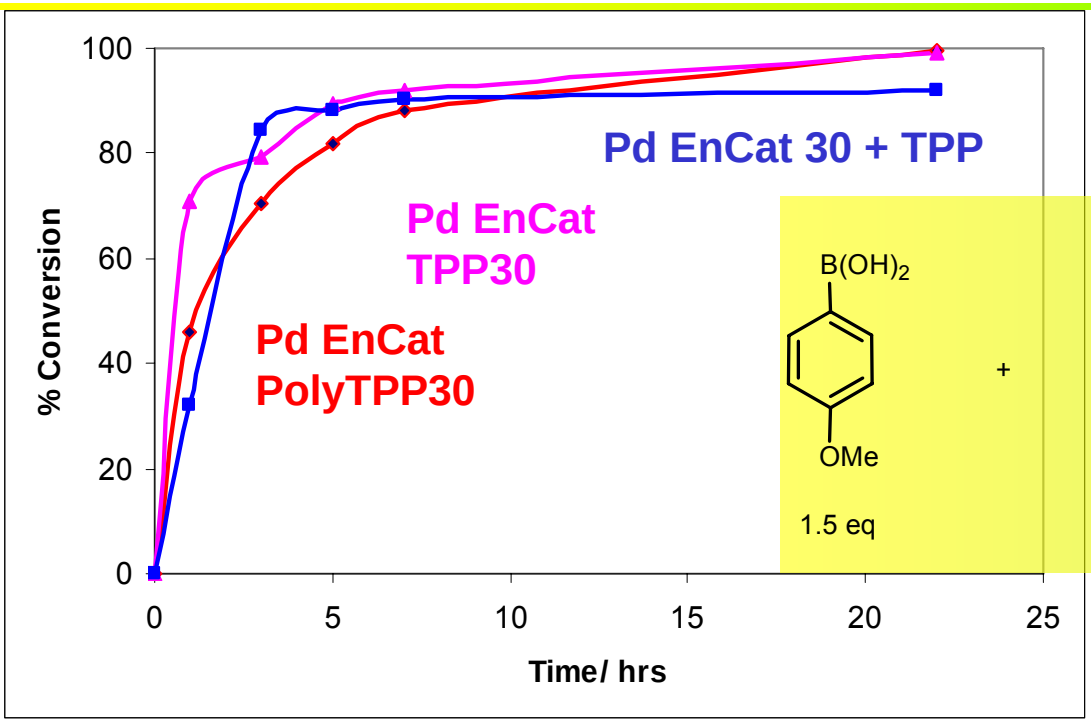
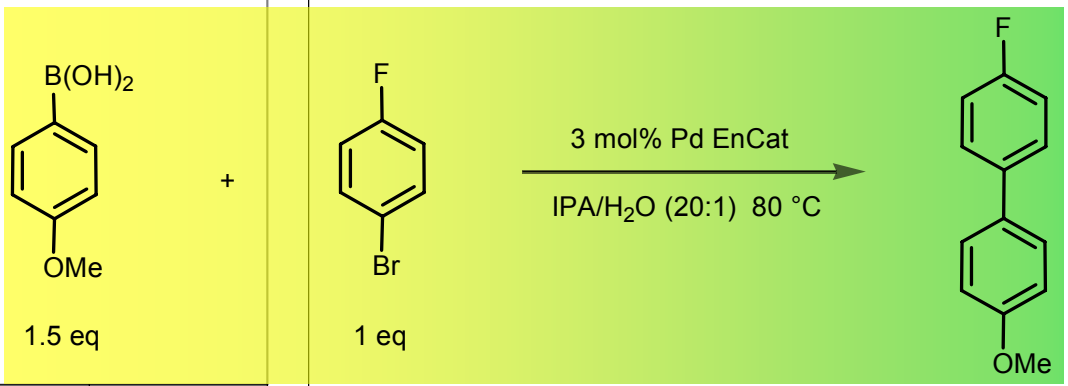
Micro EnCat™





	Pd EnCat™ PolyTPP30	Pd EnCat™ TPP30	Pd EnCat™ 30 + TPP
Product Yield (%)	99	96	92
Pd in crude product (ppm)	7	36	73
P in crude product (ppm)	18	58	430

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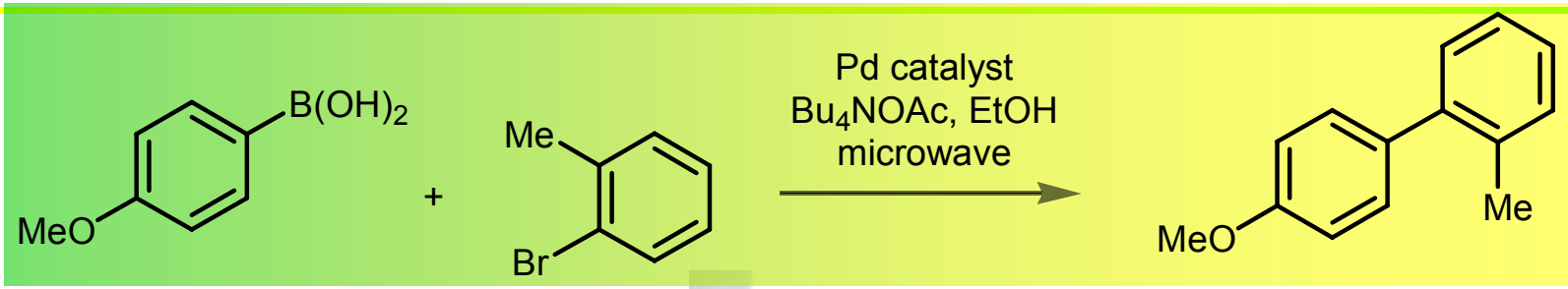
Micro EnCat™



$Pd(OAc)_2$, 5 mol%
140 °C, 25 min, 61%

Micro EnCat, 5 mol%
140 °C, 25 min, 92%

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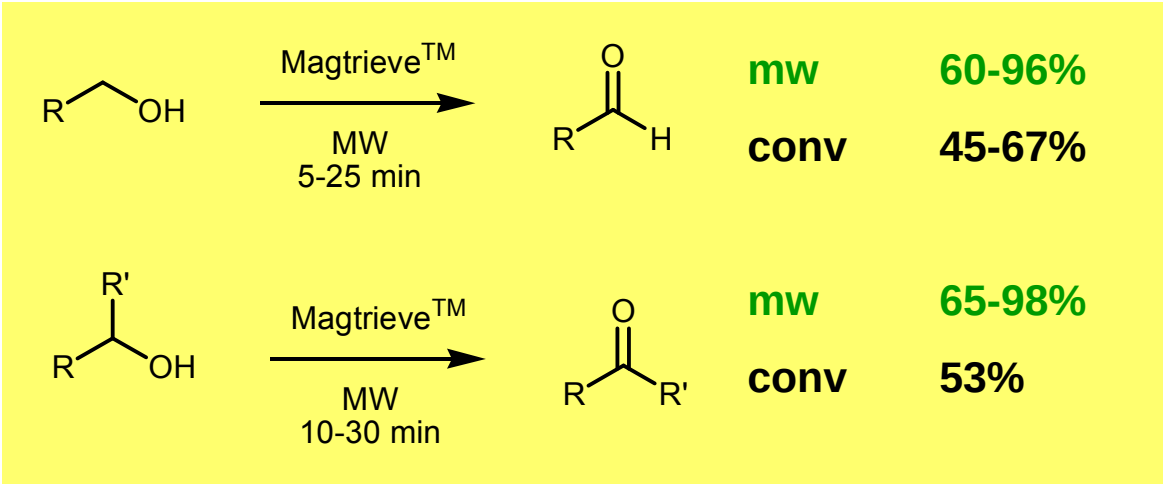
info@reaxa.com

selective microwave heating of catalysts



- **heterogeneous oxidation catalyst (Magtrieve™, CrO_2) was heated to 140 °C in a toluene suspension**
- **uniform and rapid heating (360 °C in 2 min on dry solid)**

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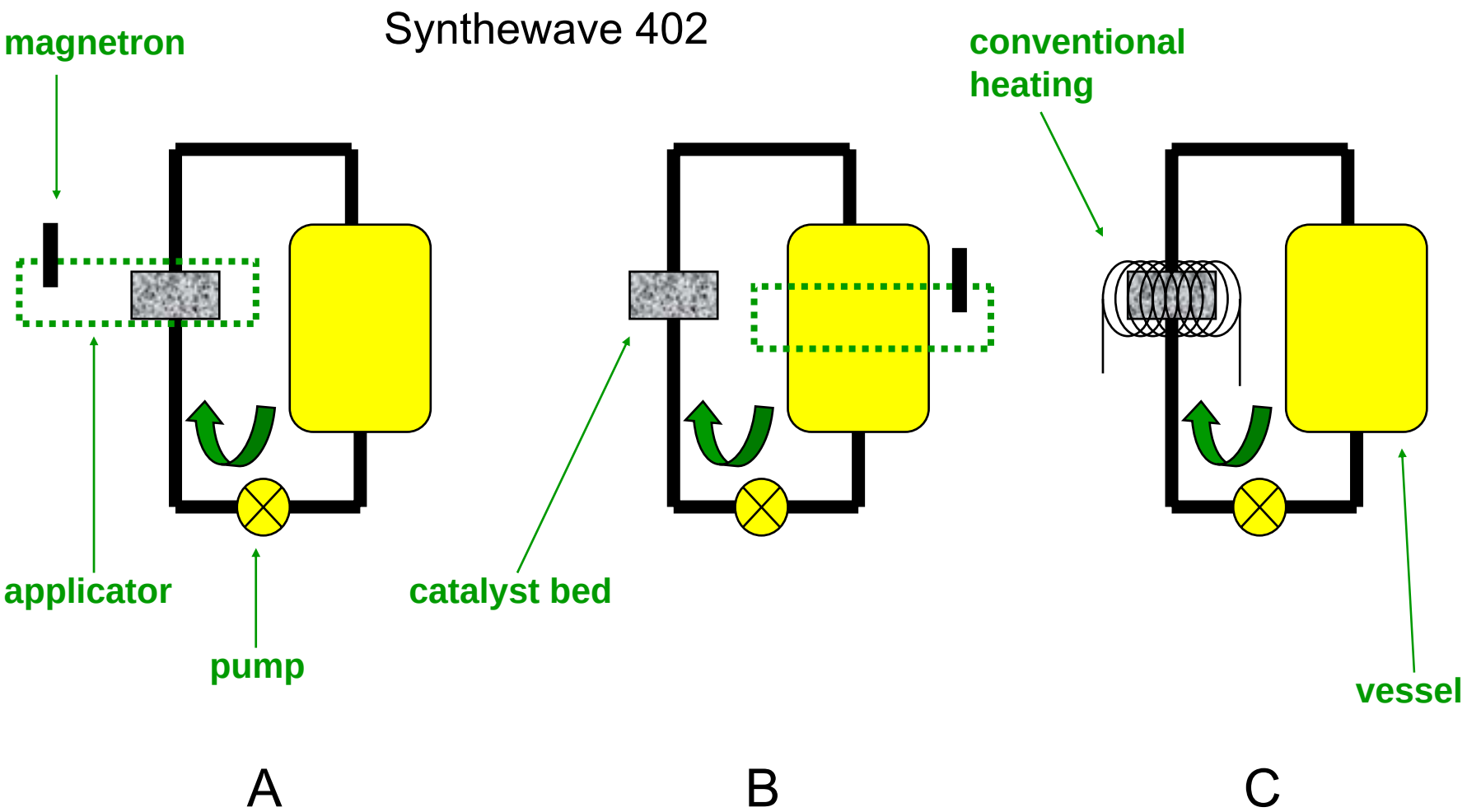
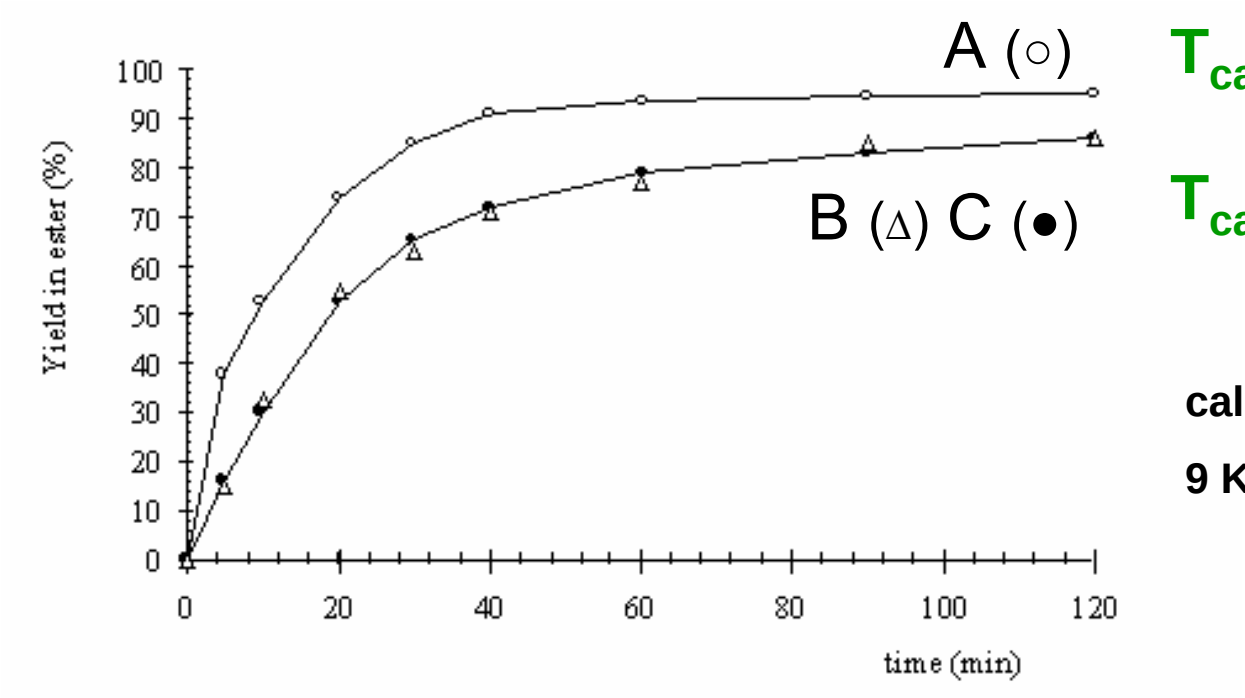
Bogdal *et. al., Adv. Synth. Catal.*, 2003, **345**, 1269

selective microwave heating of catalysts



Chemat & Esveld, www.mdpi.net/ecsoc-5/e0017/e0017.htm
J. Microwave Power Electromag. Energy, 1998, 88

selective microwave heating of catalysts



$T_{cat} > T_{bulk}$

$T_{cat} = T_{bulk}$

calculated:

9 K difference

reaction is a simple esterification,
with a granulated ceramic catalyst

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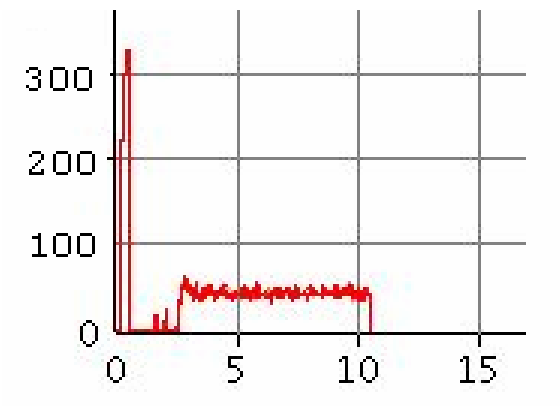
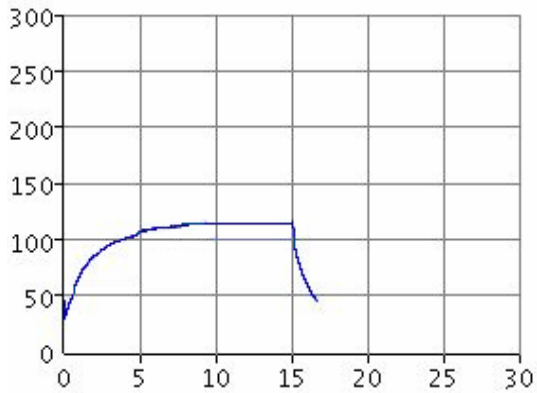
Chemat & Esveld, www.mdpi.net/ecsoc-5/e0017/e0017.htm
J. Microwave Power Electromag. Energy, 1998, 88

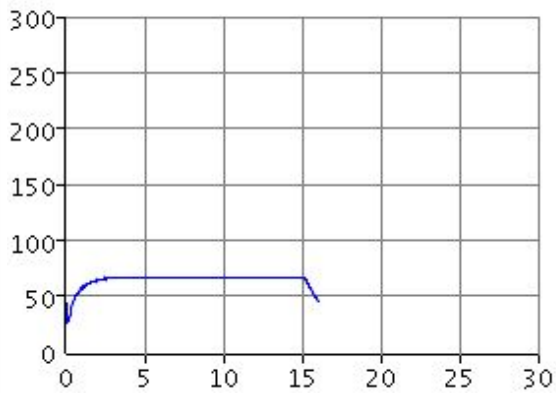
simultaneous cooling



power profile for 120 °C



50 W
15 min

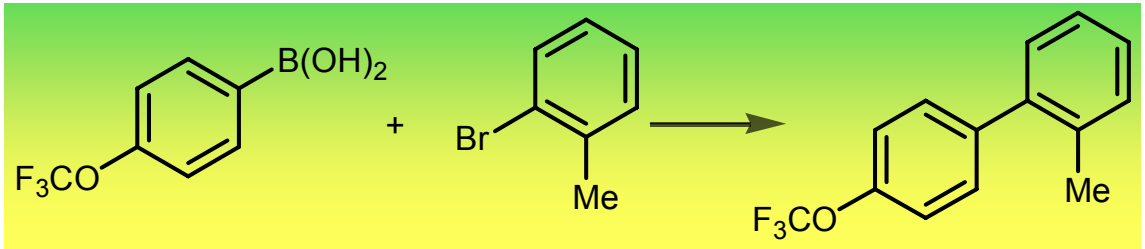


50 W + cooling
15 min

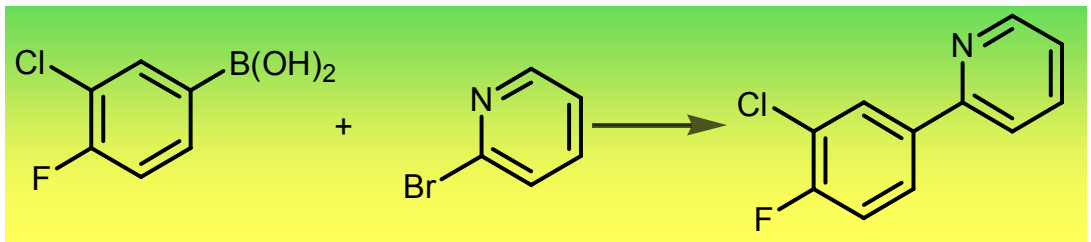
temperature of Pd catalyst inside beads

T_{cat} >>> T_{bulk} ?

simultaneous cooling



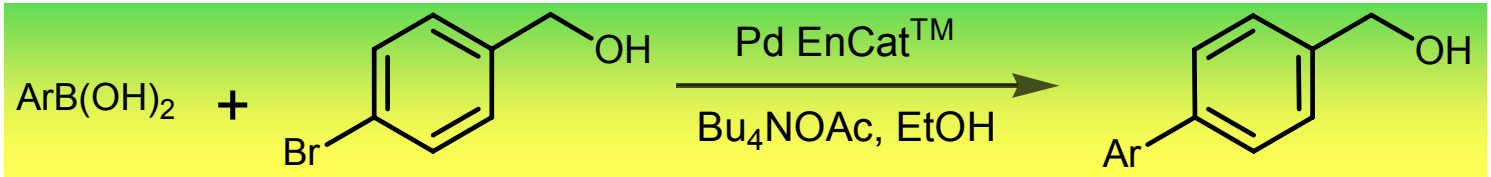
120 °C, 10 min **purity 48%**
50 W, 15 min with cooling **purity >98%**
(max. temp. 76 °C)



120 °C, 10 min **purity ~15%**
50 W, 15 min with cooling **purity >98%**
(max. temp. 76 °C)

0.5 mmol halide, 0.5 mmol boronic acid, 1.0 mmol Bu_4NOAc, 0.025 mmol Pd EnCat™, EtOH, microwave irradiation purity measured by LCMS and ^1H NMR.

simultaneous cooling



Ar	purity	
	120 °C	50 W with cooling
Ph	46%	>98%
3,4,5-$(MeO)_3$Ph	>10%	88%
4-(F_3CO)Ph	32%	86%
3-O_2NPh	31%	94%
2-benzofuranyl	41%	97%
3-quinolinyl	>10%	81%
2-thiophenyl	no reaction	no reaction

0.5 mmol halide, 0.5 mmol boronic acid, 1.0 mmol Bu_4NOAc,
0.025 mmol Pd EnCat™, EtOH, microwave irradiation
purity measured by LCMS and ^1H NMR.

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