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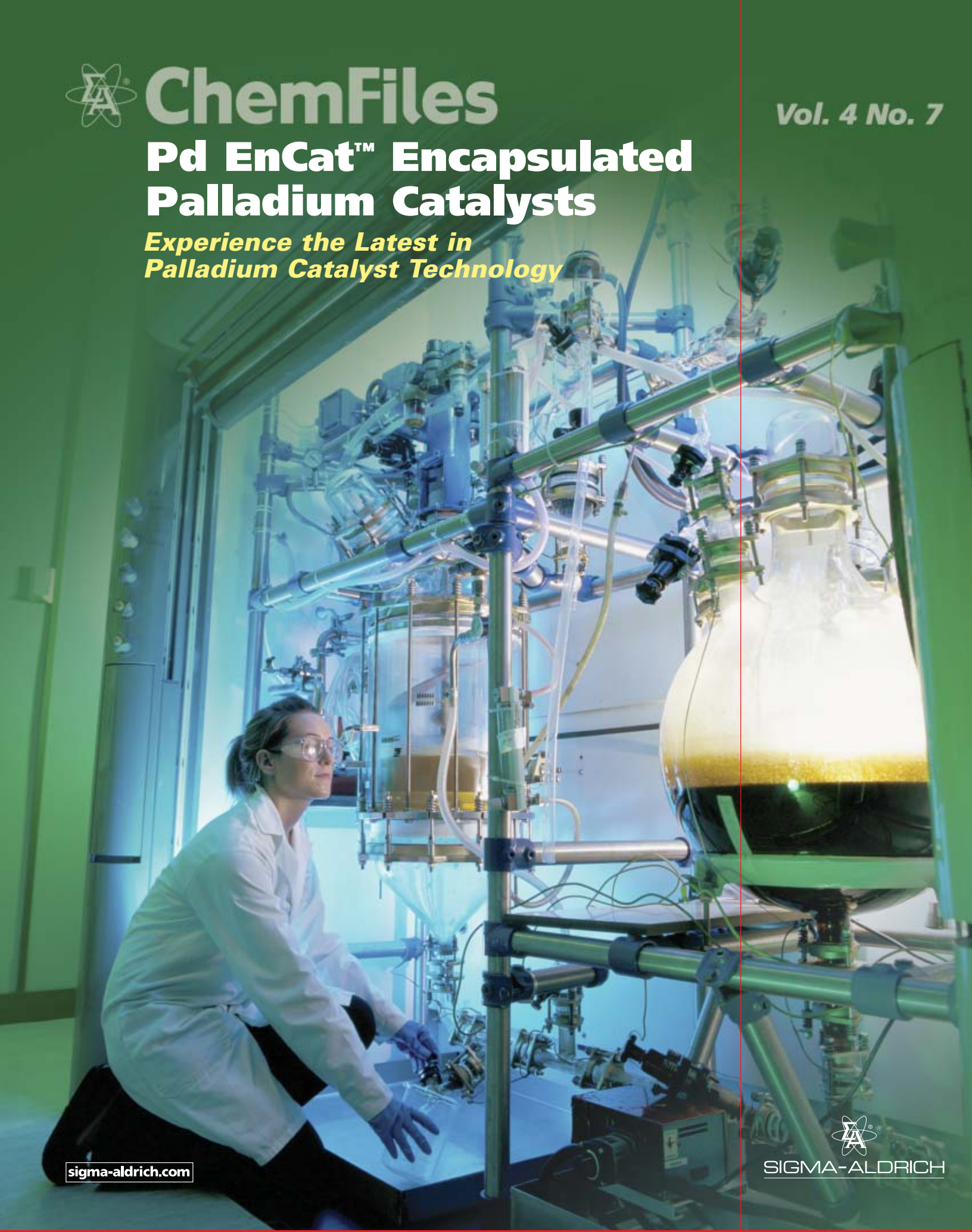
Vol. 4 No. 7

Pd EnCat™ Encapsulated Palladium Catalysts

Experience the Latest in Palladium Catalyst Technology



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Sigma-Aldrich is pleased to announce an agreement with Avecia to distribute Pd EnCat™ encapsulated palladium catalysts worldwide.

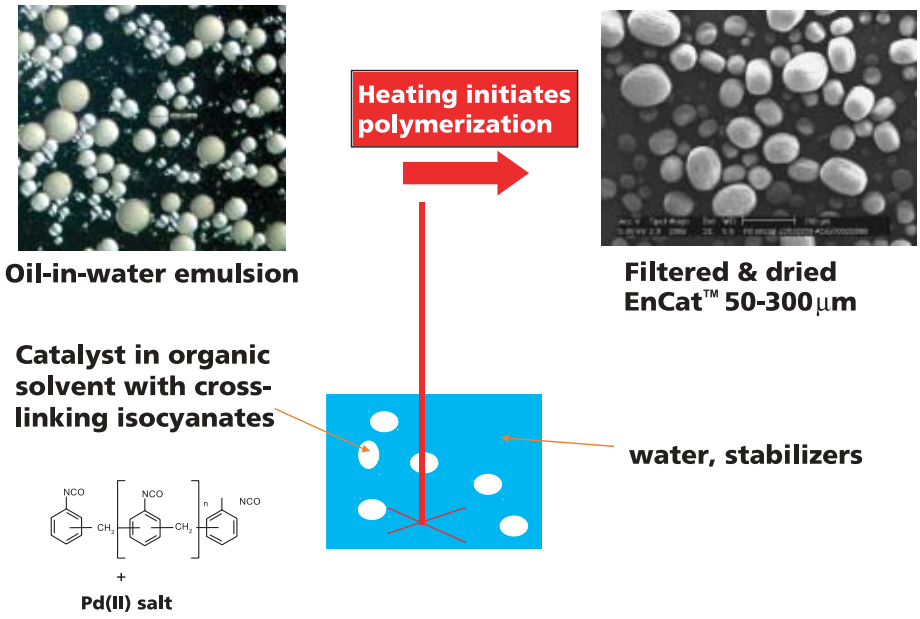
Homogeneous palladium catalysts are widely utilized due to their versatility, reactivity and functional group tolerance. However, using homogeneous catalysts presents some problems including:

- Probable palladium contamination of product necessitating additional clean up
- Palladium contamination of process equipment with associated decontamination costs
- Heavy metal contamination of waste streams from extraction and washing solvents
- Cost of catalyst lost during reaction and reaction work-up

Pd EnCat™ addresses these issues by using microencapsulation technology to immobilize the palladium, optionally with activating ligands, within a highly crosslinked polyurea matrix.

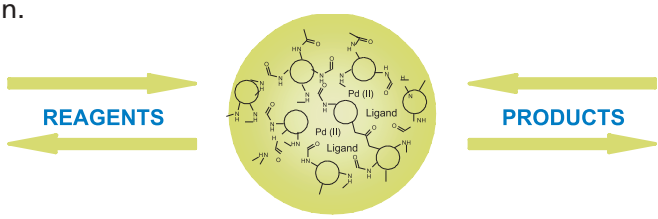
How it's Made

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



How it works

Substrates access the catalytic palladium sites by diffusion through the porous polyurea matrix; the metal remaining captured within.



Advantages Of Pd EnCat™ Catalysts

- Low residual metal levels in final crude product (typically <10ppm before purification)
- Easy recovery of catalyst by filtration
- Safer and easier to handle than palladium on carbon
- Compatibility with a wide range of process technology options e.g. fixed bed, fluidized bed, trickle bed and microwave reactors
- Efficiency and economy gains through recovery and recycling
- No plating out of palladium on vessel walls

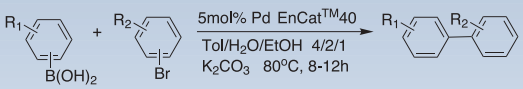
Images Courtesy of Avecia
www.avecia.com

Pd EnCat™ Applications

The performance of Pd EnCat™ is well-documented in an array of widely used transformations. The applications range from C-C bond forming processes, including **Suzuki**, **Heck**, **Carbonylation**, **Sonogashira**, and **Stille** coupling, to reductions of carbonyls, alkenes, nitro groups, and epoxides[1-9]. Selected examples are shown in *Tables 1-7*. Pd EnCat™ are available optionally with co-encapsulated ligands (*Table 2*) which simplifies removal of not only Pd but also ligand. Remarkably, these immobilized catalysts mediate high yield transformations often without significant increase in reaction times.

Table 1 Suzuki Coupling

Pd EnCat™40 Catalyzed Suzuki Couplings



R_1	R_2	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

Table 2 Suzuki Coupling with Co-encapsulated Phosphines

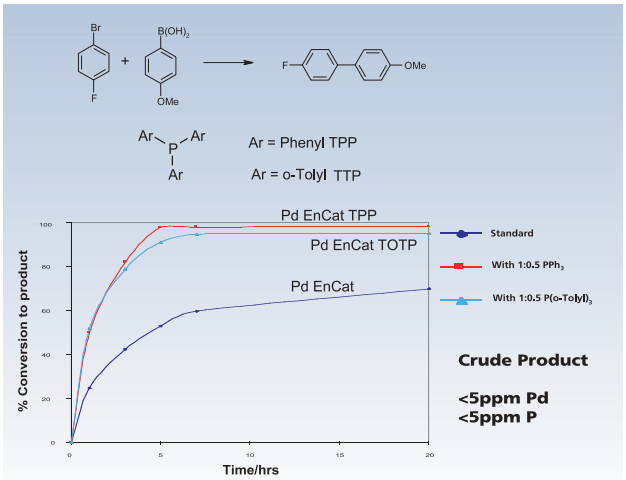
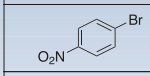
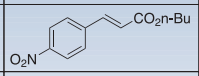
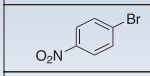
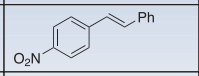
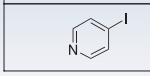
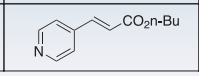
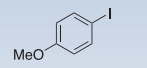
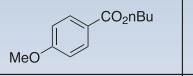
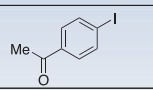
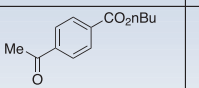
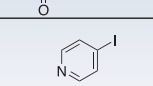
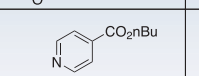


Table 3 Heck Reaction

Substrate	Product	Yield
		91%
		93%
		98%

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

Table 4 Carbonylation

Substrate	Product	Yield
		99%
		95%
		93%

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

Transfer hydrogenations eliminate the need for an external source of hydrogen gas and are readily carried out using nanoparticulate encapsulated Pd(0), Pd(0) EnCat™ 30NP[1,6]. This unique catalyst is significantly easier to use and safer to handle than activated palladium on carbon. *Table 5* illustrates the mild conditions, high yields, and chemoselectivities achieved in the **reduction** of *p*-nitroacetophenone and benzylic epoxides. As with other Pd EnCat™, Pd(0) EnCat™ 30NP is highly recyclable without significant loss of activity as shown (*Table 6*). Alternatively, chemoselective hydrogenations may be carried out by pre-activation of Pd EnCat™ to give Pd(0) EnCat™, yielding an immobilized palladium zero catalyst which facilitates high yields and excellent chemoselectivities in a variety of reductions (*Table 7*)[2].

Resistance to leaching Pd is a key advantage of the Pd EnCat™ products. Levels of Pd found in crude product are dependent on solvent (*Table 8*), substrate, and reaction conditions. Typically the Pd level in crude product is 10-20ppm prior to any purification. However, levels can be higher or lower and solvent selection is key to achieve minimum leaching; avoiding DMF and DMA where possible. Pd EnCat™ strongly resist swelling in the majority of solvents (*Table 9*) which is particularly important for scale up applications.

Table 5 Transfer Hydrogenation with Pd(0) EnCat™30 NP

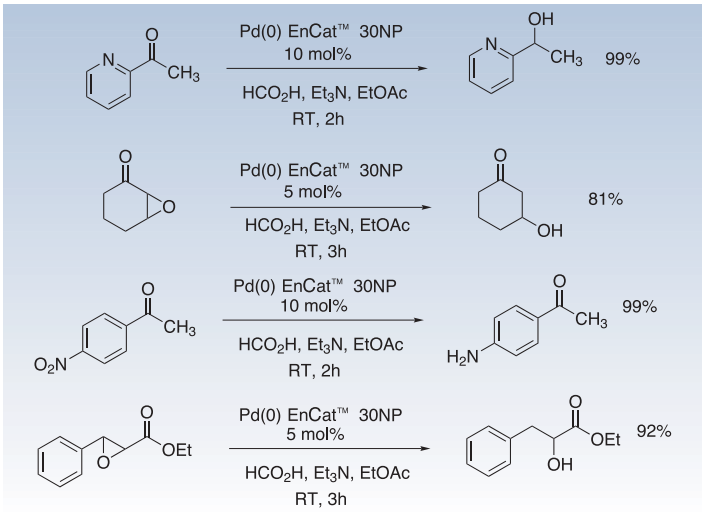


Table 7 Hydrogenation

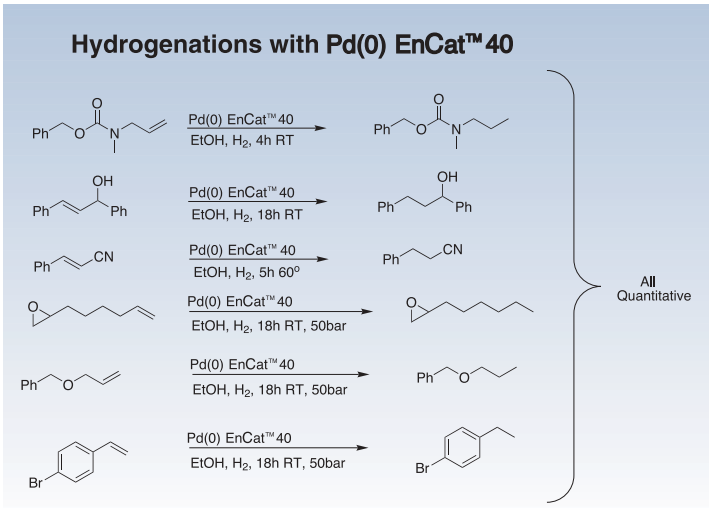


Table 9 Resistance to Swelling

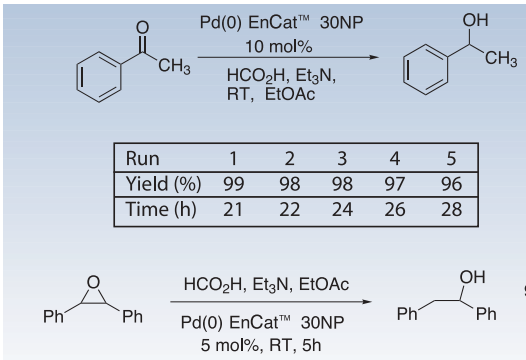
Solvent Swelling of Pd EnCat™ 40

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

Solvent swell determined by measuring gain in volume of 1g sample of beads in solvent at room temperature over 2h, expressed as %.

All Pd EnCat™ contain $Pd(OAc)_2$ except Pd(0) EnCat™ 30NP

Table 6 Recyclability



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

Pd(0) EnCat™ 30NP recycled ten times without significant loss of activity

Table 8 Resistance to Leaching

Leaching of Pd from Pd EnCat™ (ppm)

Solvent	Pd EnCat™ 40	Pd EnCat™ 30
THF	1	4
Acetone	<1	1
Ethanol	<1	<1
Acetonitrile	1	<1
IPA	<1	<1
Toluene	<1	<1
Dioxane	1	<1
Ethyl acetate	<1	<1
DMF	7	5
DMA	6	3

Pd EnCat™ (0.3g, 0.4 mmol/g) was weighed in to a 25ml carousel reaction tube and the solvent (20ml) added. The mixture was then heated to 80°C whilst stirring via magnetic stirrer for 2 days. The mixture was allowed to cool to room temperature and filtered through a sintered funnel. The filtrate was collected and analysed for Pd content.

Frequently Asked Questions

Are there significant differences between Pd EnCat™ 30 and Pd EnCat™ 40?

While Pd EnCat™ 40 shows excellent performance in a variety of transformations, Pd EnCat™ 30, with lower matrix content, shows similar performance but with improved kinetics while maintaining the mechanically robust nature of Pd EnCat™ 40 under similar conditions. End users are encouraged to screen the sample sets for best fit to application.

What if I would like a different matrix porosity, a different ligand, or a different metal?

Avecia and Sigma-Aldrich intend to collaborate on extensions to the product line.
Requests for custom EnCat™ should be directed to Avecia at *encat@avecia.com*.

Can you provide additional information on using Pd EnCat™?

As a supplement to the referenced literature below, request a free copy of the EnCat™ Users Guide on CD via e-mail at *cdavis1@sial.com*.

Save by purchasing Pd EnCat™ sample sets:
One set of 1g of each for $250.00
(mention code PRO100300)
One set of 10g of each for $1,999.00
(mention code PRO100299)
(For USA customers only)

Available Pd Encat™ Products

Name	Matrix Content (%)	% Pd (mmol/g)	P (mmol/g)	Ligand	Units
64,472-2 Pd EnCat™ 40	40	3.9–4.6(0.4)	N/A	N/A	1g
64,471-4 Pd EnCat™ 30	30	3.9–4.6(0.4)	N/A	N/A	1g
64,470-6 Pd EnCat™ TPP30	30	3.9–4.6(0.4)	0.26–0.35	Ph_3P	1g
64,469-2 Pd EnCat™ TOTP30	30	3.9–4.6(0.4)	0.15–0.20	$(o\text{-tolyl})_3P$	1g
65,366-7 Pd(0) EnCat™ 30NP, Wet *(45% water, unit weight excludes water)*	30	3.7–4.6(0.4)	N/A	N/A	1g

Pd EnCat™ technology, international patent applications have been applied for by Avecia including PCT/GB 02/03135
Pd EnCat™ was first commercialized by Avecia following a highly successful research collaboration with Professor Steven Ley from Cambridge University and teams from Syngenta and AstraZeneca.

For bulk inquiries, please call us at 800-336-9719 (USA)
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