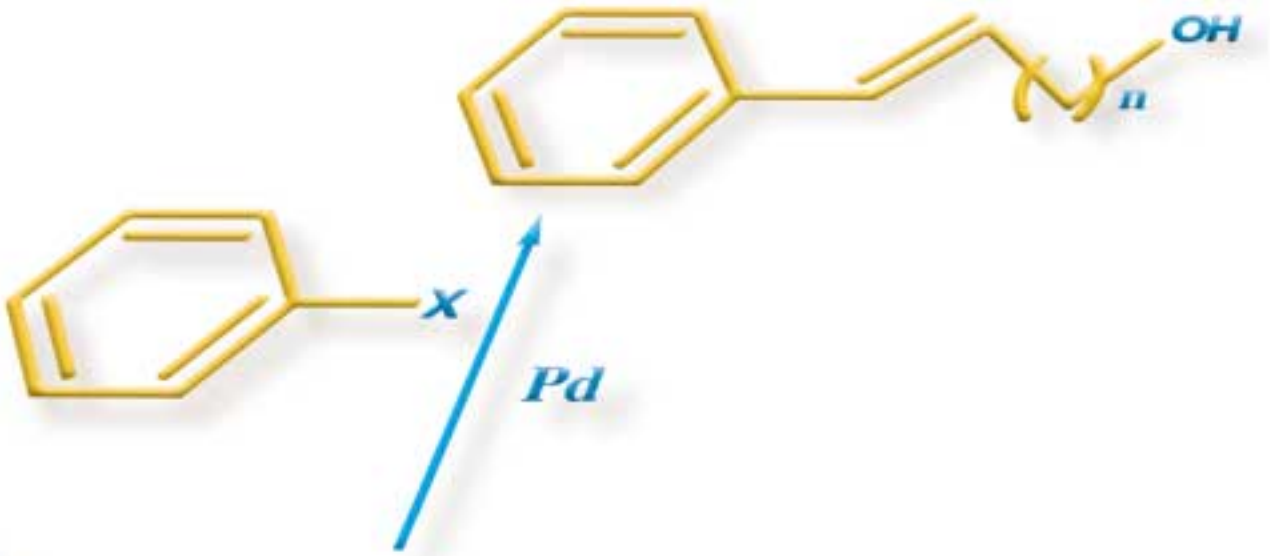
Johnson Matthey

be selective



new catalyst developments for cross-coupling reactions

Johnson Matthey: a world leader in Precious Metals

Established nearly 200 years ago, Johnson Matthey continues to be at the forefront in developing the chemistry of the platinum group metals. As the sole marketing agent for Anglo American Platinum Corporation, the largest platinum mining group in the world, we offer the assurance of continued supply of precious metals.

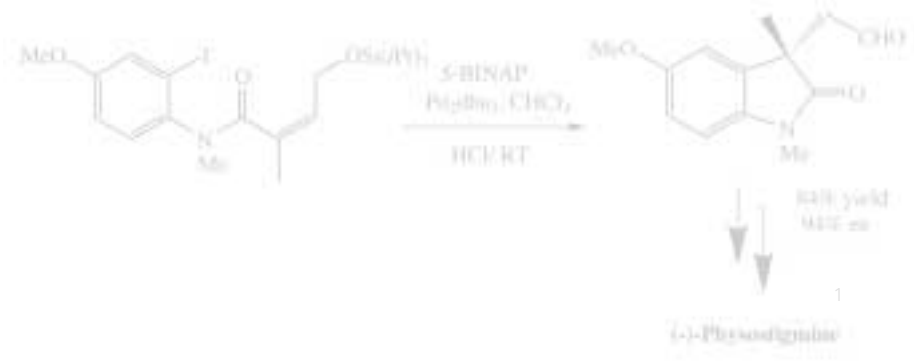
Within Johnson Matthey Chemicals Division we manufacture and supply, up to bulk quantities, a range of platinum group metal heterogeneous catalysts, homogeneous catalysts and chemical compounds. We continue to innovate catalyst technologies, such as the recent introduction of FibreCat® anchored homogeneous catalysts. This range offers the selectivity of a homogeneous catalyst with the ease of separation and handling of a heterogeneous system.

Catalysts can be purchased individually or in the form of a screening kit for you to evaluate. The kits contain a wide range of catalysts allowing immediate availability of a selection of suitable catalysts for screening. Johnson Matthey can also carry out catalyst screenings for customers, through the Catalytic Services business. This is a new contract service enabling optimal catalytic process selection, offering a faster, more cost effective way to the catalytic solution.

Precious metal recovery is a key component of the whole process. We have recently introduced a new metal scavenging technology, Smopex®, for fast and efficient removal of precious metals from catalytic processes. Smopex® fibres are highly functionalised polymers that allow easy purification of your product by removal of the precious metal.

Johnson Matthey continues to develop its total refining service and is introducing new technologies to further improve the recycling of your precious metal.

New catalyst developments for cross-coupling reactions



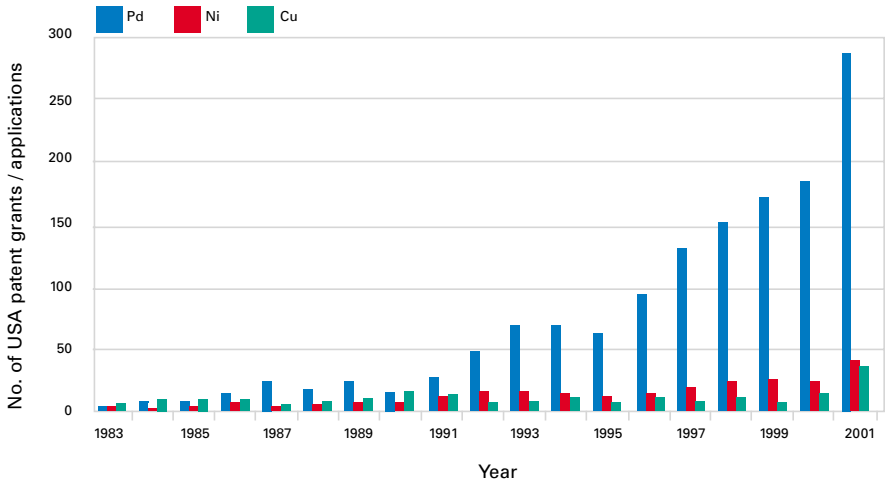
References:
1) S. Brase and A. deMeijere in *"Metal-catalyzed Cross-coupling Reactions"* ed., F. Diederich and P.J. Stang, Wiley-VCH, Weinheim, 1997.

❶ Introduction

Palladium catalysts in coupling chemistry

Interest in coupling reactions has been steadily increasing over the past twenty years as shown in the graph below. There are many reasons why this has been the case:

- the synthetic routes are reliable and allow the convergent synthesis of complex target molecules.
- the same syntheses can be carried out more efficiently using a much smaller number of reaction steps.
- coupling reactions with palladium use clean, efficient chemistry.



In response to this growing interest, Johnson Matthey has a wide range of catalysts available for use in C-C, C-N, C-O, C-S coupling reactions such as Heck, Suzuki and Sonogashira. All of these catalysts are prepared via scalable routes and, with the exception of the FibreCat® catalysts which are available solely from Johnson Matthey, all are non-proprietary catalysts.

We are also continually developing new catalysts to meet the demands of the more complex coupling reactions. At Johnson Matthey, we have been focusing our attention on developing increasingly sophisticated catalysts whilst optimising the manufacturing scale of the existing product range.

New catalysts now available NEW

Pd (I) Dimer: $[Pd(P^tBu_3)(\mu\text{-}Br)]_2$

Highly active catalyst that shows particularly good activity for difficult aminations and heteroaryl couplings.

$Pd(PCy_3)_2Cl_2$

A new catalyst containing PCy_3, one of the few phosphines that activates alkyl halides towards coupling chemistry.

Triaryl phosphite based palladacycle

A catalyst offering greatly increased turnover numbers.

FibreCat®

Polymer anchored homogeneous catalysts – offer the activity and selectivity of conventional homogeneous catalysts whilst allowing easy separation from the reaction medium.

❷ Types of catalysts for cross-coupling reactions

The types of catalysts available at Johnson Matthey are shown below:

Pd precursors

e.g. $[Pd(OAc)_2]_3$, $Pd(dba)_x$, generally used with a suitable ligand system.

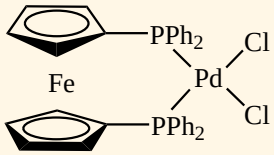
1st Generation catalysts

simple PPh_3 based Pd catalysts.

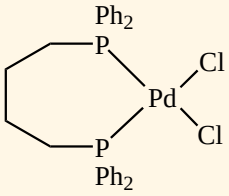
e.g. $Pd(PPh_3)_4$, *trans*-$[Pd(PPh_3)_2Cl_2]$.

2nd Generation catalysts

e.g. $Pd(P(o\text{-tol})_3)_2Cl_2$ or bidentate phosphine-palladium complexes:



$Pd(dppf)Cl_2$

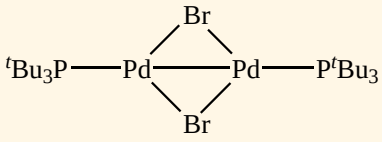


$Pd(dppb)Cl_2$

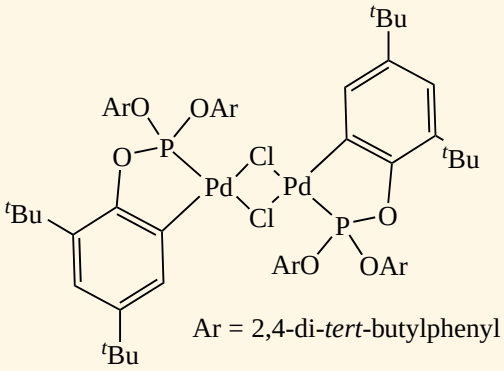
3rd Generation catalysts

NEW

eg. Pd (I) dimer, $Pd(PCy_3)_2Cl_2$, Triaryl phosphite based palladacycle.



Pd (I) dimer

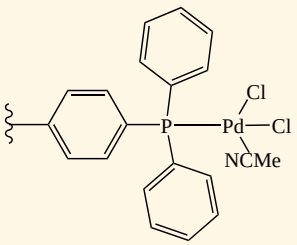


Ar = 2,4-di-*tert*-butylphenyl

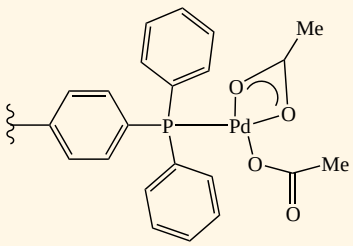
Triaryl phosphite based palladacycle

Anchored Pd catalysts – FibreCat®

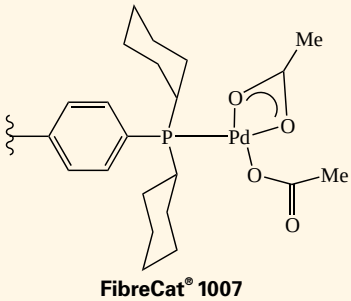
NEW



FibreCat® 1026
PPh_2-fibre / $PdCl_2$ / MeCN



FibreCat® 1001
PPh_2-fibre / $Pd(OAc)_2$



FibreCat® 1007
PCy_2-fibre / $Pd(OAc)_2$

JM

❸ Choosing the right catalyst for your cross-coupling reaction

Reaction type/ substrate	Compound number	Alkyl Halide Coupling Reactions	Aryl Chloride Coupling Reactions	Aryl Amination/ Ketone Arylation ①	Aryl/ Vinyl Bromide and Iodide substrates		
					Challenging Coupling Reactions ②	Standard Coupling Reactions ③	Simple Coupling Reactions ④
Pre-formed catalysts							
$[Pd(P^tBu_3)(\mu\text{-}Br)]_2$	Pd-113	✗	✓✓✓	✓✓✓	✓✓✓	✓✓✓	✓✓✓
$Pd(PCy_3)_2Cl_2$	Pd-114	✓✓✓	✓✓	✓✓	✓✓	✓✓✓	✓✓✓
$Pd(P(o\text{-}tol)_3)_2Cl_2$	Pd-115	✗	✓✓	✓✓	✓✓	✓✓✓	✓✓✓
$[Pd(P(OPh\text{-}2,4\text{-}^tBu_2)_3)Cl]_2$	Pd-109	✗	✓	✓	✓✓✓	✓✓✓	✓✓✓
FibreCat® 1007		✗	✓✓	✓✓	✓✓✓	✓✓✓	✓✓✓
FibreCat® 1026		✗	✓	✓	✓✓	✓✓✓	✓✓✓
FibreCat® 1001		✗	✓	✓	✓✓	✓✓✓	✓✓✓
$Pd(dppf)Cl_2$	Pd-106 Pd-107	✗	✓	✓✓	✓✓	✓✓✓	✓✓✓
$Pd(dppb)Cl_2$ **$Pd(dppe)Cl_2$**	Pd-105 Pd-103	✗	✓	✓	✓✓	✓✓✓	✓✓✓
$Pd(PPh_3)_4$	Pd-101	✗	✗	✓	✓	✓✓	✓✓
$Pd(PPh_3)_2Cl_2$	Pd-100	✗	✗	✓	✓	✓✓	✓✓
Pd precursors							
$[Pd(OAc)_2]_3$ **$Pd(dba)_x$** **$[Pd(\pi\text{-}C_3H_5)Cl]_2$** **$Pd(acac)_2$** **$Pd(MeCN)_2Cl_2$** **$PdCl_2$**	Pd-111 Pd-92 Pd-110 Pd-70 Pd-62	✗	✗	✗	✗	✗	✓
(with added ligand)		(✓)	(✓)	(✓✓)	(✓✓)	(✓✓✓)	(✓✓✓)

✓✓✓ Shows very high activity and high turnover rates in the specified reaction
✓✓ Shows good activity and reasonable turnover rates in the specified reaction
✓ Shows some activity for specified reaction
✗ Shows little or no activity for the specified reaction

①Amination refers to "Buchwald/ Hartwig amination." Ketone Arylation includes other carbonyl functionality, eg. ester, amide etc.
②Challenging couplings include electron-rich or sterically hindered aryl/ vinyl bromides or iodides.
③Standard couplings are generally electron-neutral aryl/ vinyl bromides or iodides.
④Simple couplings are generally electron-poor aryl/ vinyl bromides or iodides.

❹ Screening capabilities

All of the catalysts listed are available now for use in customer reactions. Depending on customer requirements the catalysts can be purchased individually, in the form of a kit for testing in-house, or a catalyst screen can be set up at Johnson Matthey.

Screening Kits

Catalyst kits can be purchased from Johnson Matthey for customer screening in cross coupling reactions. These allow the customer to have:

> A broad range of catalysts, stored in one place, which are readily available when required for screening in house, proving them to be an essential addition to your laboratory.

Johnson Matthey currently has two kits available containing catalysts for coupling reactions. One kit is specifically designed to meet the needs of the chemist carrying out more complex coupling reactions and the other offers a range of catalysts for simpler coupling reactions.

Catalytic Services

Johnson Matthey Catalytic Services offers a contract service for the screening of catalysts on your behalf whereby we can develop and optimise your catalytic processes for you. The service includes:

- rapid evaluation of the viability of the catalyst step
- early identification of optimum catalyst
- development of scalable catalytic routes

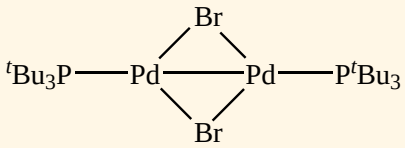
Use Johnson Matthey's experience in catalysis to deliver efficient, viable, scalable coupling steps.

❺ New Catalysts

a. Palladium (I) tri-*tert*-butylphosphine bromide dimer

Pd113: $[Pd(P^tBu_3)(\mu\text{-}Br)]_2$

Johnson Matthey offers this rare example of a palladium (I) compound.[1] It is a highly active catalyst for coupling reactions and will activate aryl chlorides and sterically hindered or electron rich aryl bromides.[2] It is especially active in difficult aminations and heteroaryl halide couplings, has very fast turnover rates and is easy to handle.



Johnson Matthey offers this rare example of a palladium (I) compound.

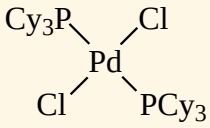
The high activity and fast turnover rates achievable were illustrated in the recent results from the laboratory of Prof. John Hartwig, Yale University.[3] These showed that the rate of conversion to product was **significantly faster** using Pd-113: $[Pd(P^tBu_3)(\mu\text{-}Br)]_2$ than when using $Pd(P^tBu_3)_2$ or $Pd(dba)_2$ / P^tBu_3 as catalyst in the amination of 3-bromothiophene.

References:
1) M. Mingos *et al, J.Chem.Soc.Dalton Trans.*, **1996**, 23, 4313; M. Mingos *et al, Chem.Commun.* **2000**, 16, 1525.
2) G. Fu *et al, JACS*, **2000**, 4020; G. Fu *et al, Angew. Chem. Int. Ed.*, **1999**, 2411; J. Hartwig *et al, JACS*, **1999**, 3224; J. Hartwig *et al, JACS*, **1998**, 7369.
3) J. Hartwig *et al, unpublished results*, **2001**.

⑤ New Catalysts *(continued)*

b. Dichlorobis (tricyclohexylphosphine) Palladium (II)
Pd 114: $Pd(PCy_3)_2Cl_2$

This is a new highly active, general coupling catalyst which provides the unique activity of PCy_3 in a convenient, air-stable form. This palladium/ phosphine system has recently been shown to catalyse a wide range of coupling reactions,[4] and is also one of the first ever catalysts for the coupling of alkyl halides.[5] It provides a commercially viable solution to many of the more challenging coupling reactions.

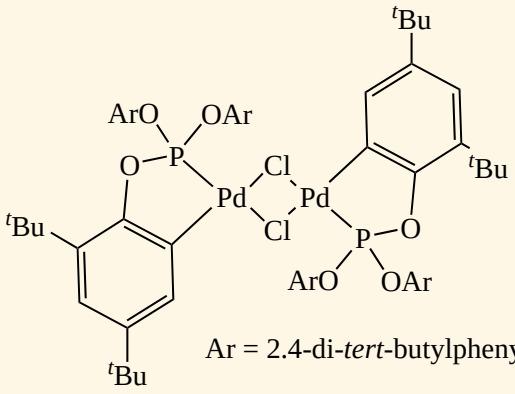


One of the first ever catalysts for the coupling of alkyl halides.

References:
4) G. Fu *et al, JACS*, **2000**, 4020.
5) G. Fu *et al, Angew. Chem. Int. Ed.*, **2002**, 1945.

c. Triaryl phosphite based palladacycle
Pd-109: $[Pd(P(OPh\text{-}2,4\text{-}^tBu_2)_3)Cl]_2$

We have available commercially a new palladacycle catalyst containing the tris(2,4-di-*tert*-butylphenyl)phosphite ligand. This shows very high activity and turnover rates, with catalyst loadings of 10^{-4} mol% used for certain reactions.[6,7] The catalyst exhibits good air and thermal stability, and is supplied as an off-white powder.



Ar = 2.4-di-*tert*-butylphenyl

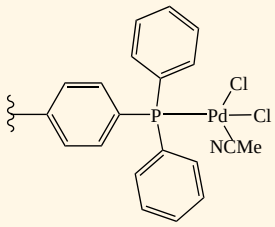
Shows very high activity and turnover rates.

References
6) R. Bedford *et al, Chem. Commun.*, **1998**, 2095.
7) R. Bedford *et al, Tett. Lett.*, **1998**, 9793.

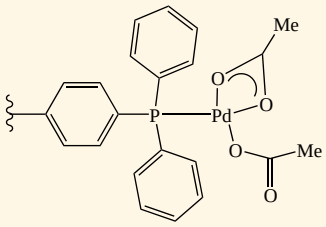
⑤ New Catalysts *(continued)*

d. Anchored Pd catalysts - FibreCat® 1000 series

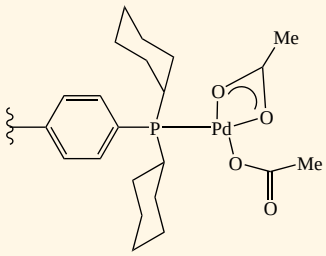
Levels of metal leaching are minimised when using FibreCat®



FibreCat® 1026
PPh_2-fibre / $PdCl_2$/ MeCN

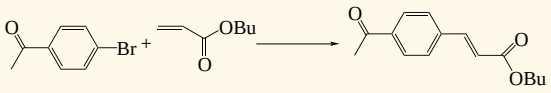


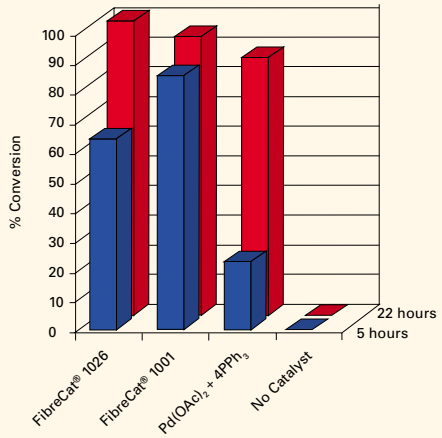
FibreCat® 1001
PPh_2-fibre / $Pd(OAc)_2$



FibreCat® 1007
PCy_2-fibre / $Pd(OAc)_2$

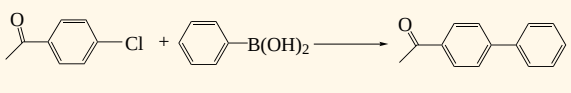
This is a new range of polymer anchored homogeneous catalysts. These products show good activities and enhanced selectivities compared to conventional homogeneous catalysts in both simple and complex coupling reactions. They can also be easily separated from the reaction mixture and owing to the strong nature of the bond between the catalyst and the fibre, the levels of metal leaching are minimised.

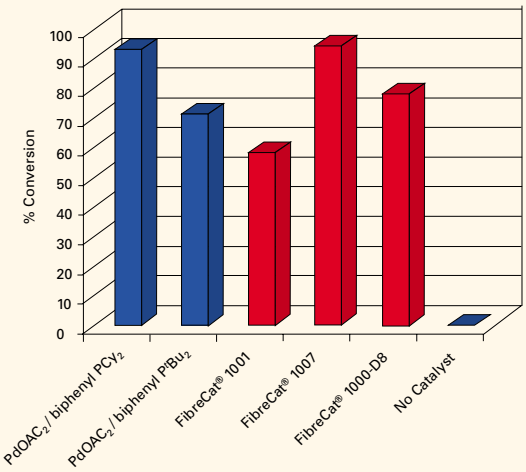




Conditions: 100°C, DMA, NaOAc, 0.25 mol% Pd

Graph 1 shows the rate of reaction and activities obtained when using FibreCat® 1026 and 1001 in a bromo Heck reaction.





Conditions: 90°C, Toluene, KF, 1 mol% Pd, 24 hrs

Graph 2 shows the rate of reaction and activities obtained when using FibreCat® 1007 and 1000–D8 in a chloro Suzuki reaction.

We are constantly developing new FibreCat® products in the US and UK. Some examples are FibreCat® 1000-D8 (a ^{t}Butyl-phosphine based system), and FibreCat® products involving Pd(π-allyl)Cl (Pd [II]) and $Pd(dba)_x$ (Pd [0]). We can use our Fibre technology to anchor your catalyst of choice. Please talk to us about developing a system tailored to your requirements.

❻ Product purification and recovery of precious metals

Johnson Matthey offers a total service to its customers. As well as supplying a complete range of precious metal catalysts, we also have available advanced techniques to recover and recycle precious metals from spent catalysts.

New options for product purification: Smopex®

NEW

The separation of a homogeneous catalyst from a reaction medium is often difficult. Johnson Matthey can now offer a way to remove the metal from your solution without the need for expensive and time consuming recrystallisation steps.
By introducing the **Smopex®** range of high capacity functional fibres for precious metal scavenging we are able to offer:

- excellent kinetics – metal recovery is achieved in minutes particularly in the presence of excess phosphines
- easy separation to leave a clean product
- improved product yields

We have a range of Smopex® fibres available suited to recovery of precious metals from coupling residues.

New advances in metal recovery

The process economics of catalytic reactions are influenced by the extent to which the precious metal can be recycled. Johnson Matthey offers two alternative routes for the recovery of the metal.

- We have a state of the art refining service to treat coupling residues allowing the efficient recycling of the precious metal. This includes AquaCat®, Johnson Matthey's newest refining technology, which is a 'closed loop' system for sampling and recovery of catalyst residues.
- In addition it is now feasible to recover low levels (ppm levels) of precious metals from catalyst streams using Smopex®. Due to the faster kinetics and higher capacities that the fibres offer we are able to scavenge metal much more effectively than current scavenging technologies.

❼ Catalysts in development

Johnson Matthey is constantly updating and developing new highly active palladium catalysts for use in coupling chemistry. We are currently developing a range of Pd (II) and Pd (0) catalysts based on commercially available phosphines, that show novel activity profiles and will enable the fast and effective application of coupling reactions from laboratory to production scale.

Contact us

Johnson Matthey has an expert team available to discuss your particular requirements in confidence. Please contact us now (see back cover) and find out more about how we can help you get the most from your coupling reactions.

www.chemicals.matthey.com

Product Range

Catalogue No.	Compound	Formula	CAS No.
Pd-62	*trans*-dichlorobis(acetonitrile) palladium (II)	*trans*-$[Pd(CH_3CN)_2Cl_2]$	14592-56-4
Pd-70	bis(acetylacetonato) palladium (II), $Pd(acac)_2$	$Pd(C_5H_7O_2)_2$	14024-61-4
Pd-92	(dibenzylideneacetone) palladium (0), $Pd(dba)_X$	$Pd(C_{17}H_{14}O)_X$	51364-51-3
Pd-100	*trans*-dichlorobis(triphenylphosphine) palladium (II)	*trans*-$[Pd(PPh_3)_2Cl_2]$	13965-03-2
Pd-101	tetrakis(triphenylphosphine) palladium (0)	$Pd(PPh_3)_4$	14221-01-3
Pd-102	diacetato(1,3-bis(diphenylphosphino)propane) palladium (II), $Pd(dppp)(OAc)_2$	$Pd(Ph_2PCH_2CH_2CH_2PPh_2)(OAc)_2$	149796-59-8
Pd-103	dichloro(1,2-bis(diphenylphosphino)ethane) palladium (II), $Pd(dppe)Cl_2$	$Pd(Ph_2PCH_2CH_2PPh_2)Cl_2$	19978-61-1
Pd-105	dichloro(1,4-bis(diphenylphosphino)butane) palladium (II), $Pd(dppb)Cl_2$	$Pd(Ph_2PCH_2CH_2CH_2CH_2PPh_2)Cl_2$	29964-62-3
Pd-106	dichloro(1,1′-bis(diphenylphosphino)ferrocene) palladium (II), dichloromethane adduct $Pd(dppf)Cl_2.CH_2Cl_2$	$Pd(Ph_2PC_5H_4FeC_5H_4PPh_2)Cl_2.CH_2Cl_2$	95464-05-4
Pd-107	dichloro(1,1′-bis(diphenylphosphino)ferrocene) palladium (II), $Pd(dppf)Cl_2$	$Pd(Ph_2PC_5H_4FeC_5H_4PPh_2)Cl_2$	72287-26-4
Pd-109	di-μ-chlorobis(tri(2,4-di-*tert*-butylphenyl)phosphite-2-C,P) dipalladium (II)	$[Pd(P(OPh\text{-}2,4\text{-}^tBu_2)_3)Cl]_2$	217189-40-7
Pd-110	palladium (II) (π-allyl) chloride dimer	$[Pd(\pi\text{-}C_3H_5)Cl]_2$	12012-95-2
Pd-111	palladium (II) acetate trimer hexakis (μ-acetato) tripalladium (II)	$[Pd(OAc)_2]_3$	53189-26-7
Pd-113	palladium (I) tri-*tert*-butylphosphine bromide dimer	$[Pd(P^tBu_3)(\mu\text{-}Br)]_2$	185812-86-8
Pd-114	dichlorobis(tricyclohexylphosphine) palladium (II) $Pd(PCy_3)_2Cl_2$	$Pd(P(C_6H_{12})_3)_2Cl_2$	29934-17-6
Pd-115	dichlorobis(tri-*ortho*-tolylphosphine) palladium (II), $Pd(P(o\text{-}tol)_3)_2Cl_2$	$Pd(P(C_7H_7)_3)_2Cl_2$	40691-33-6
	palladium (II) chloride	$PdCl_2$	7647-10-1
FibreCat® 1026	palladium chloride on triphenylphosphine functionalised fibre		
FibreCat® 1001	palladium acetate on triphenylphosphine functionalised fibre		
FibreCat® 1007	palladium acetate on dicyclohexylphenylphosphine functionalised fibre		

FibreCat® anchored homogeneous catalysts are prepared by anchoring a range of Pd precursors to a series of functionalised fibres.

Product range

This list is not exhaustive and is constantly being updated. Please contact us if there is a co-ordination compound that you are particularly interested in which is not listed.

For further information please contact your local sales representative or:

Europe
Johnson Matthey Chemicals
Orchard Road, Royston,
Hertfordshire SG8 5HE
United Kingdom

Tel: +44 (0)1763 253000
Fax: +44 (0)1763 253573

Email: chemicals@matthey.com
Web: www.chemicals.matthey.com

United States
Johnson Matthey Chemicals
2001 Nolte Drive, West Deptford,
New Jersey 08066 1727
United States of America

Tel: +1 856 384 7151
Fax: +1 856 384 7282

Email: catinquiries@jmusa.com
Web: www.chemicals.matthey.com

Asia
Johnson Matthey Japan Inc.
Nishishimbashi Tokyu Building
3-16-11 Nishishimbashi, Minato-ku
Tokyo 105-0003
Japan

Tel: +81 3 5776 6164
Fax: +81 3 5776 6162

Email: onumar@matthey.com
Web: www.jmj.co.jp