Empowering Cross-Coupling

Buchwald G1 to G6 Pre-Catalysts

2025 Edition

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Introduction

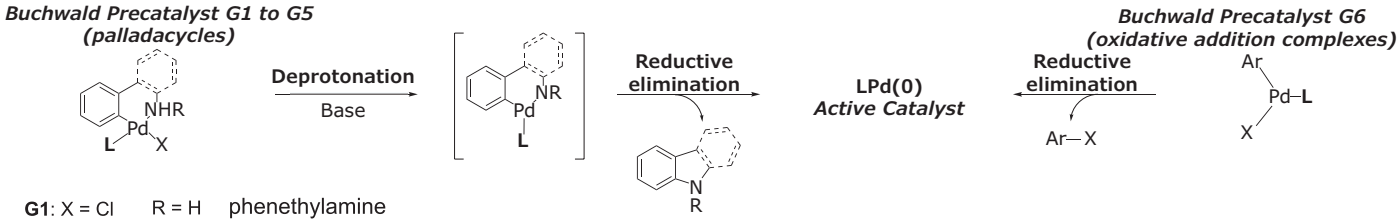
Efficient generation of the active catalyst is often pivotal to the success of a cross-coupling reaction. Traditional palladium sources, such as $Pd_n(dba)_m$ (n = 1 or 2, and m = 2 or 3, respectively),[1] Pd(II) salts,[2] and π-allyl Pd dimers,[3] can have varying degrees of efficacy in generating LPd(0) active catalyst species.

To help you achieve success in cross-coupling reactions, and the new chemistry you're engaged in, we offer a comprehensive range of G1 to G6 Buchwald pre-catalysts. The series consists of Pd(II) complexes comprised of highly active, versatile, and tunable biarylphosphine ligands, or other highly active phosphine ligands, capable of efficiently catalyzing C–C,[4] C–N,[5] C–O,[6] C–F,[7] C–CF_3,[8] C–S,[9] and other bond formations.[10]

All Buchwald G1 to G6 pre-catalysts are air-, moisture-, and thermally-stable; display good solubility in common organic solvents; and support a wide array of phosphine ligands. In general, these robust pre-catalysts allow diverse reactivity, accurate control of the ligand-to-palladium ratio, efficient formation of LPd(0) species under mild conditions, low catalyst loadings, and short reaction times.

Discover our unparalleled Buchwald portfolio for your breakthrough ideas.

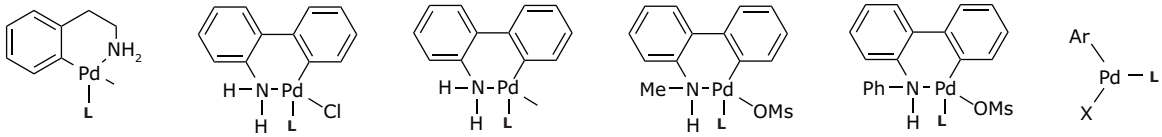
Activation of G1 to G5 Pre-Catalysts vs. G6 Pre-Catalysts



G1: X = Cl R = H phenethylamine
G2: X = Cl R = H aminobiphenyl
G3: X = OMs R = H aminobiphenyl
G4: X = OMs R = Me aminobiphenyl
G5: X = OMs R = Ph aminobiphenyl

Generic Structures & Descriptions of G1 to G6 Pre-Catalysts

Structure:



Generation	**Pd G1**	**Pd G2**	**Pd G3**	**Pd G4**	**Pd G5**	**Pd G6**
Disclosure Year:	2008	2010	2013	2014	2014	2017

Pd G1

The first generation (G1) pre-catalysts[11] allow for easy generation of LPd(0) species, requiring merely a deprotonation with an amide base (below room temperature), an alkoxide base (at room temperature), or a carbonate base (at elevated temperature). The resulting catalytic species is very active, even at temperatures near -40 °C, and can be used in a variety of cross-coupling protocols.

Pd G2

The second generation (G2) pre-catalysts[12] contain an aminobiphenyl scaffold rather than the phenethylamine scaffold of G1 pre-catalysts. This change allows for the use of weak phosphate or carbonate bases to generate LPd(0) species from G2 pre-catalysts at room temperature. These catalysts prove remarkably adept at achieving a variety of cross-coupling reactions.

Pd G3

G1 and G2 pre-catalysts can suffer from limitations related to their syntheses and/or application scope. Replacing the chloride anion of the G2 pre-catalysts with a more electron-withdrawing, non-coordinating methanesulfonate anion provides the third generation (G3) pre-catalysts, which can accommodate very bulky ligands (e.g., t-BuBrettPhos).[13] In addition, these pre-catalysts show long life in solution and exhibit enhanced versatility, as they are highly soluble in a wide variety of common organic solvents.

Pd G4 and Pd G5

In rare cases, the carbazole leaving group generated from activation of G3 pre-catalysts can inhibit catalytic activity by consuming valuable reaction feedstock, and complicate workup/purification. To circumvent this issue, the Buchwald group prepared fourth generation (G4) and fifth generation (G5) pre-catalysts[14] by methylating and arylating the amino group on the aminobiphenyl scaffold, respectively. Compared to G3 pre-catalysts, G4 and G5 exhibit higher solubilities while maintaining excellent catalytic activity. However, G4 and G5 pre-catalysts of extremely bulky ligands (e.g., RockPhos and AlPhos) are only formed with great difficulty.

Pd G6

Overall, sixth generation (G6) pre-catalysts[15] are superior to earlier Buchwald pre-catalysts. First, G6 pre-catalysts are highly versatile, because each of the three ligands (anionic ligand **X**, phosphine ligand **L**, and aryl scaffold **Ar**) of the oxidative addition complexes (OACs) can be independently tuned to create a nearly endless number of pre-catalyst variations. Therefore, improved solubility, greater stability, increased reactivity, and/or easier purification can be achieved through careful design or selection of these three components. Second, G6 pre-catalysts are very reactive because these OACs are presumptive intermediates on the catalytic cycle for cross-coupling processes. In fact, unlike G1 through G5, the activation of G6 pre-catalysts to LPd(0) species does not require a base. Third, G6 pre-catalysts demonstrate clear superiority over G3 pre-catalysts, as their activation produces only harmless by-products. Fourth, G6 pre-catalysts outperform G4 and G5 pre-catalysts due to their ability to easily accommodate very bulky ligands. Fifth, stability studies have shown that G6 pre-catalysts remain stable in air within a benchtop desiccator for over a year and can be handled outside of a glovebox, similar to G1 through G5 pre-catalysts. Additionally, multiple reports have directly compared the performance of G6 pre-catalysts with earlier generations across various cross-coupling reactions, revealing that G6 pre-catalysts typically exhibit enhanced reactivity, selectivity, reaction scope, and/or yields.[5,9,15]

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Product List

Ligand Name	Ligand No.	G1	G2	G3	G4	G6	G6 OTf/ TES	(L)PdCl$_2$	(L)Pd (crotyl)	(L)$_2$Pd	(L)$_4$Pd
Biaryl Ligands											
SPhos	**638072**	**704946**	**753009**	**776246**	**804282**	**931853**					
XPhos	**638064**	**704954**	**741825**	**763381**	**804274**	**937460**					
RuPhos	**663131**	**707589**	**753246**	**763403**	**804290**	**938742**					
t-BuXPhos	**638080**	**708739**		**762229**							
BrettPhos	**718742**	**718750**		**761605**	**804355**						
t-BuBrettPhos	**730998**			**745979**		**912646**	**912883**				
AdBrettPhos	**768154**			**776106**		**915378**					
AdCyBrettPhos	**900278**					**925454**					
CPhos	**759171**		**763012**	**763004**	**900471**						
(*t*-Bu)PhCPhos	**900275**			**900534**	**900533**						
RockPhos	**791016**			**773905**		**937428**					
Me$_4$*t*-BuXPhos	**675938**			**900620**							

Ligand Name	Ligand No.	G1	G2	G3	G4	G6	G6 OTf/ TES	$(L)PdCl_2$	(L)Pd (crotyl)	$(L)_2Pd$	$(L)_4Pd$
Biaryl Ligands											
Me_3(OMe)*t*-BuXPhos	**792470**			**804193**							
DavePhos	**638021**			**804959**	**900702**						
PhDavePhos	**695882**										
t-BuDavePhos	**695874**			**903701**	**903663**						
JohnPhos	**638439**										
CyJohnPhos	**638099**		**747807**	**900621**	**900284**						
MePhos	**695262**										
t-BuMePhos	**695211**										
JackiePhos	**731013**			**762830**							
TrixiePhos	**710342**			**796530**							
VPhos	**900331**			**901219**							
EPhos	**901215**			**936170**	**901220**	**938734**					
sSPhos	**677280**		**763314**								
CPhos-JackiePhos hybrid	**900277**										
AlPhos	**799718**					**915602**	**916455**				
GPhos	**918008**			**920460**	**920479**	**922900**					
APhos (AmPhos)	**677264**		**764299**	**764183**	**900608**	**938823**					
MorDalPhos	**751618**			**792357**	**900276**						
^{me}CgPPh	**695459**		**761281**	**762822**							
JosiPhos SL-J009-1	**88733**			**747130**							
JosiPhos SL-J009-2	**88734**			**RNI00044**							
rac-BINAP	**481084**			**804967**	**900340**						
(*R*)-Tol-BINAP	**693049**			**905607**	**900472**						
cataCXium® A	**671479**		**761311**	**761435**	**900349**						
AndrewPhos	**918997**										
SummerPhos	**918989**										
(*R*)-AntPhos	**913456**										
(*S*)-AntPhos	**912476**										
VincePhos	**918970**										
AliPhos	**919004**										
EvanPhos	**902292**										
*t*BuSPhos	**944254***			944300*	944297*	944319*					
(*R*)-BIDIME	**913200**										
CM-Phos	**752231**										
(*S*)-BIDIME	**912719**										
5-[Bis(1,1-dimethylethyl) phosphino]-1-(1-naphthalenyl)-1H-pyrazole	**710598**										
HandaPhos	**799580**										

*Coming soon

Ligand Name	Ligand No.	G1	G2	G3	G4	G6	G6 OTf/ TES	$(L)PdCl_2$	(L)Pd (crotyl)	$(L)_2Pd$	$(L)_4Pd$
Symmetrical Phosphine Ligands											
$(t\text{-Bu})_2PMe$	**642629**			**901194**	**900700**						
$(t\text{-Bu})_2PPh$	**682411**			**901197**	**900699**						
$P(Ad)_3$	**924350**										
$P(Mes)_3$	**395080**										
$P(o\text{-Tol})_3$	**287822**		**759163**							**711071**	
$P(t\text{-Bu})_3$	**570958**		**756482**	**804851**	**900701**	**931586**				**676578**	
PCy_3	**261971**		**756741**	**764175**	**900287**			403237			
PPh_3	**T84409**		**752762**					**208671**			**216666**
Tri(2-furyl)phosphine	**383767**										
Tri-1-naphthylphosphine	**667218**										
Tris(1-pyrrolidinyl) phosphine	**775444**										
Water Soluble Phosphine Ligands											
PTABS	**926760**										
1,3,5-Triaza-7-phosphaadamantane	**695467**										
sSPhos	**677280**		**763314**								
Triphenylphosphine-3,3′,3′′-trisulfonic acid trisodium salt	**744034**										
Chelating Xanthene Based Ligands											
N-XantPhos	**666564**			**794228**	**900455**						
t-Bu-XantPhos	**667196**										
XantPhos	**526460**		**763047**	**763039**	**900329**						
BippyPhos Ligands											
AdBippyPhos	**740845**							**903124**			
BippyPhos	**676632**										
CyBippyPhos	**738611**										
Ylide-Functionalized Phosphine Ligands											
joYPhos™	**912042**										
keYPhos™	**913294**										
trYPhos™	**913030**										
DalPhos Ligands											
CyPAd-DalPhos	**910732**										
PAd_2-DalPhos	**919551**										
PAd-DalPhos	**900593**										
PhPAd-DalPhos	**910724**										

Ligand Name	Ligand No.	G1	G2	G3	G4	G6	G6 OTf/ TES	$(L)PdCl_2$	(L)Pd (crotyl)	$(L)_2Pd$	$(L)_4Pd$
Chelating Phophine Ligands with Alkyl Chains											
dcpe	**479500**										
dppe	**376728**										
dppp	**262048**										
Tris[2-(diphenylphosphino) ethyl]phosphine	**327697**										
Chelating Ferrocene-Based Phosphine Ligands											
1,1′-Bis(diis-opropylphosphino) ferrocene	**578266**							**702005**			
CyMPhos	**923478**										
DPPF	**177261**			**804983**	**900454**			**697230**			
DTBPF	**695149**			**804975**							
iPrMPhos	**923494**							**923508**			
PhMPhos	**923443**							**923451**			
*t*BuMPhos	**923516**							**923524**			
Other Ferrocene-Based Phosphine Ligands											
AdQPhos	**936189**			**936197**	**936200**				**936219**		
QPhos	**675784**			**903027**							
Other Ligands											
vBRIDP	**711179**										
DPEPhos	**510017**										

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