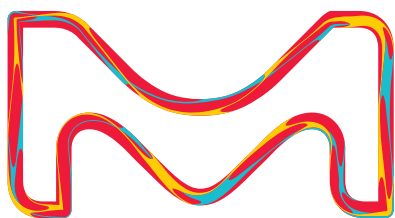


Empowering Cross-Coupling

Buchwald G1 to G6 Pre-Catalysts

2025 Edition



Professor Stephen L. Buchwald,
Camille Dreyfus Professor of
Chemistry at MIT

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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 $\text{Pd}_n(\text{dba})_m$ ($n = 1$ or 2 , and $m = 2$ or 3 , respectively),¹ $\text{Pd}(\text{II})$ salts,² and n -allyl Pd dimers,³ can have varying degrees of efficacy in generating $\text{LPd}(0)$ 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 $\text{Pd}(\text{II})$ complexes comprised of highly active, versatile, and tunable biarylphosphine ligands, or other highly active

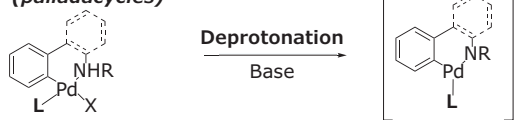
phosphine ligands, capable of efficiently catalyzing $\text{C}-\text{C}$,⁴ $\text{C}-\text{N}$,⁵ $\text{C}-\text{O}$,⁶ $\text{C}-\text{F}$,⁷ $\text{C}-\text{CF}_3$,⁸ $\text{C}-\text{S}$,⁹ and other bond formations.¹⁰

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 $\text{LPd}(0)$ species under mild conditions, low catalyst loadings, and short reaction times.

Discover our unparalleled Buchwald portfolio for your breakthrough ideas.

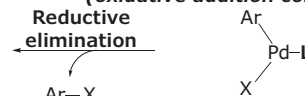
Activation of G1 to G5 Pre-Catalysts vs. G6 Pre-Catalysts

Buchwald Precatalyst G1 to G5 (palladacycles)



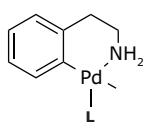
G1: X = Cl R = H phenethylamine
G2: X = Cl R = H aminobiphenyl
G3: X = OMs R = H aminobiphenyl
G4: X = OMs R = Me aminobiphenyl
G5: X = OMs R = Ph aminobiphenyl

Buchwald Precatalyst G6 (oxidative addition complexes)



Generic Structures & Descriptions of G1 to G6 Pre-Catalysts

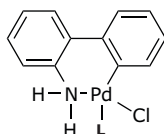
Structure:



Pd G1

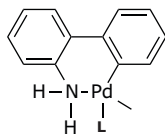
Generation
Disclosure Year:

2008



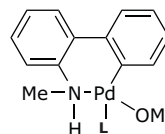
Pd G2

2010



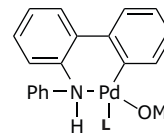
Pd G3

2013



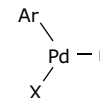
Pd G4

2014



Pd G5

2014



Pd G6

2017

Pd G1

The first generation (G1) pre-catalysts¹¹ allow for easy generation of $\text{LPd}(0)$ 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-catalysts¹² 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 $\text{LPd}(0)$ 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-catalysts¹⁴ 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-catalysts¹⁵ 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					
<i>t</i> -BuXPhos	638080	708739		762229							
BrettPhos	718742	718750		761605	804355						
<i>t</i> -BuBrettPhos	730998			745979		912646	912883				
AdBrettPhos	768154			776106		915378					
AdCyBrettPhos	900278					925454					
CPhos	759171		763012	763004	900471						
(<i>t</i> -Bu)PhCPhos	900275			900534	900533						
RockPhos	791016			773905		937428					
Me ₄ <i>t</i> -BuXPhos	675938			900620							

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											
Me ₃ (OMe) <i>t</i> -BuXPhos	792470			804193							
DavePhos	638021			804959	900702						
PhDavePhos	695882										
<i>t</i> -BuDavePhos	695874			903701	903663						
JohnPhos	638439										
CyJohnPhos	638099		747807	900621	900284						
MePhos	695262										
<i>t</i> -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							
<i>rac</i> -BINAP	481084			804967	900340						
(<i>R</i>)-Tol-BINAP	693049			905607	900472						
cataCXium® A	671479		761311	761435	900349						
AndrewPhos	918997										
SummerPhos	918989										
(<i>R</i>)-AntPhos	913456										
(<i>S</i>)-AntPhos	912476										
VincePhos	918970										
AliPhos	919004										
EvanPhos	902292										
<i>t</i> BuSPhos	944254*			944300*	944297*	944319*					
(<i>R</i>)-BIDIME	913200										
CM-Phos	752231										
(<i>S</i>)-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) ₂ Pd	(L) ₄ Pd
Symmetrical Phosphine Ligands											
(<i>t</i> -Bu) ₂ PMe	642629			901194	900700						
(<i>t</i> -Bu) ₂ PPh	682411			901197	900699						
P(Ad) ₃	924350										
P(Mes) ₃	395080										
P(<i>o</i> -Tol) ₃	287822		759163							711071	
P(<i>t</i> -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						
<i>t</i> -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) ₂ Pd	(L) ₃ Pd
Chelating Phosphine Ligands with Alkyl Chains											
dcpe	479500										
dppe	376728										
dppp	262048										
Tris[2-(diphenylphosphino)ethyl]phosphine	327697										
Chelating Ferrocene-Based Phosphine Ligands											
1,1'-Bis(diisopropylphosphino)ferrocene	578266							702005			
CyMPhos	923478										
DPPF	177261			804983	900454			697230			
DTBPF	695149			804975							
iPrMPhos	923494							923508			
PhMPhos	923443							923451			
tBuMPhos	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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