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2-Aminobiphenyl Palladacycles: The "Most Powerful" Precatalysts in C–C and C–Heteroatom Cross-Couplings

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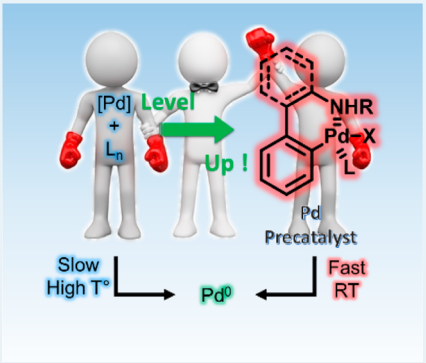
ABSTRACT: New approaches to the Pd-catalysis employing palladacycle precatalysts have been recently developed. Breakthroughs in this area using 2-aminobiphenyl palladacycle precatalysts are highlighted. High reactivity and selectivity are achieved for the C–C and C–heteroatom bond formation under mild reaction conditions.



KEYWORDS: *catalysis, palladacycles, precatalysts, C–C and C–heteroatom bonds formation, cross-couplings*

INTRODUCTION

Palladium-catalyzed coupling reactions are one of the most powerful tools for C–C and C–heteroatom bonds formation.[1] Over the past decades, this approach has emerged as a tremendously valuable synthetic method in the synthesis of sophisticated molecules with important biological or physical properties. Since the original discoveries of these reactions (Mizoroki–Heck, Suzuki–Miyaura, Stille, Negishi, Sonogashira, Buchwald–Hartwig coupling reactions, etc.), there have been significant developments in terms of better understanding the role of the palladium source and the ligand in the reaction mechanism. The steric and electronic nature of the ligand, L, and the coordination number of the Pd highly influence the outcome of the two most important steps in these couplings: the oxidative addition and the reductive elimination. The key success of such couplings is the efficient reduction of Pd(II) species, usually used, to Pd(0) and the in situ generation of the active LnPd(0) species. However, this step remains poorly understood, and the efficiency of the formation of LnPd(0) through the Pd(II)–Pd(0) reduction is not compatible with a wide range of coupling reactions. Moreover, depending on the way a palladium is mixed with a ligand, different catalytic species may be formed, which can adversely affect the activity of the catalyst and selectivity of the reaction.

One solution to this drawback is the direct use of Pd(0) sources such as commercially available $Pd(PPh_3)_4$ or $Pd_2(dba)_3$; however, in addition to their thermal instability, these Pd(0) species contain ligands complexed to Pd(0) that can interfere with the coupling by decreasing the activity of the catalyst. Thus, the "Holy Grail" is the development of new Pd-catalytic systems able to in situ generate a highly active 12-electron LPd(0) species under mild reaction conditions (room temperature and weak bases) that can achieve high conversions regardless of the nature of the coupling partners.

Breakthroughs in this area have been driven by the implementation of new classes of readily activated palladium precatalysts. Pioneering studies from Herrmann and Beller have demonstrated the capacity of cyclopalladated ligand **1** (Figure 1) to catalyze the Heck coupling with an unprecedented catalytic activity.[2] This impressive result sparked a great deal of interest among other research groups. Various cyclopalladated ligand systems have been reported and could be successfully used in C–C and C–N cross-couplings;[3] however, almost all of these precatalysts required an exogenous additive or, in some cases, one catalytic cycle to be activated.

Another category of precatalysts that has emerged as a powerful catalytic system is the recently developed Buchwald's palladacycles (Figure 1).[4] They are formed from Pd and a hemilabile ligand that subsequently dissociate during the catalytic cycle. Activation of these precatalysts may occur through the action of a suitable base to form the key intermediate palladium(II) complex **I** (Scheme 1), then the reductive elimination occurs to form the kinetically active 12-electron LPd(0) species and produces the indole/carbazole side-product in a catalytic amount.

The first and second generation (G1 and G2) of such precatalysts have shown excellent activities in Suzuki–Miyaura[5] and Sonogashira[6] couplings, amination,[7] and C–H arylation[8] reactions. For example, with the G2 precatalyst, Suzuki–Miyaura coupling reactions of five-membered 2-heterocyclic

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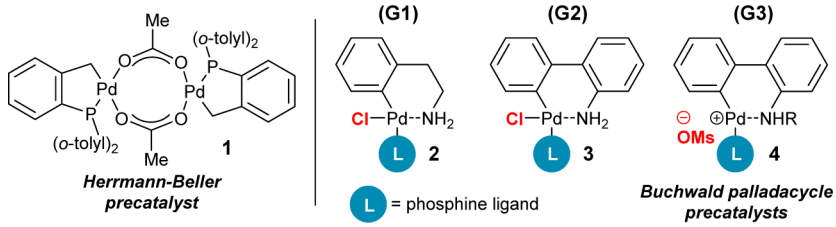
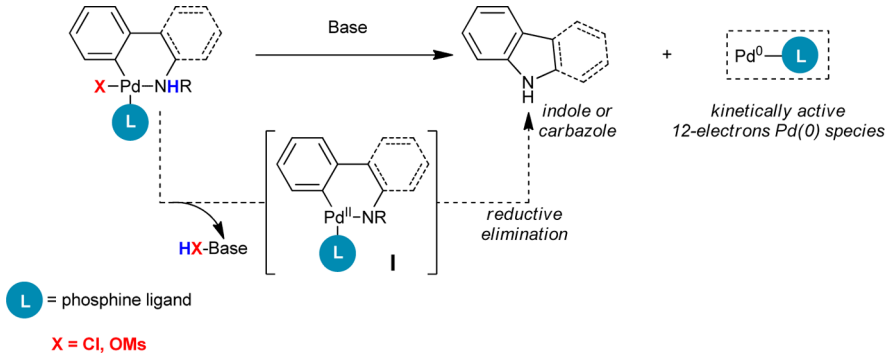
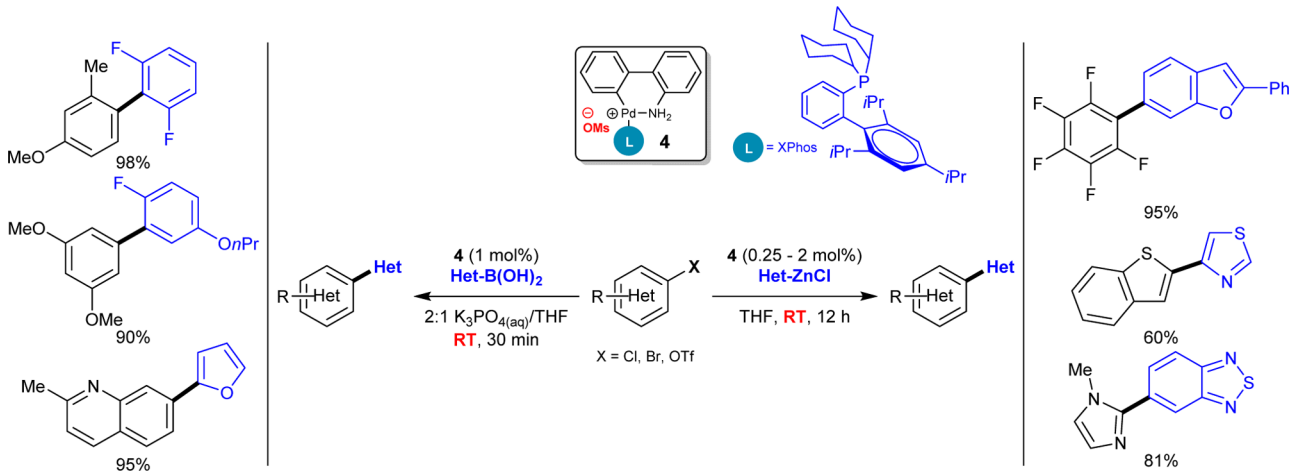


Figure 1. Herrmann–Beller precatalyst (**1**) and Buchwald precatalyst generations G1 (**2**), G2 (**3**), and G3 (**4**).

Scheme 1. General Mode of Activation of the Palladacycle Precatalysts G1, G2, and G3



Scheme 2. Use of G3-XPhos Precatalyst in Csp^2–Csp^2 Cross-Couplings



boronic acids with (hetero)aryl halides were achieved under extremely mild reaction conditions in a short reaction time.[5a] Although these first and second generations of Buchwald precatalysts exhibited a quite unique level of reactivity in coupling reactions, they still suffer from drawbacks. The first generation G1 displays a short life in solutionand cannot been activated with a weak base at room temperature, and its preparation involves the handling of unstable organometallic intermediates. For the second generation G2, in addition to being poorly soluble in organic solvents, it is also not stable in solution for extended time, and bulkier phosphines such as BrettPhos, an important ligand in C–N bond formation, *t*BuXPhos, *t*ButBrettPhos, and RockPhos could not been incorporated.

To circumvent these limitations, the Buchwald's group postulated that precatalysts of type **3** (Figure 1) based on 2-aminobiphenyl may incorporate larger ligands by rendering the Pd(II) center (i) more electron-poor through replacement of the chlorine atom with a more electron-withdrawing species and (ii) less sterically encumbered by using a noncoordinating anion. Last year, this group reported the third generation (G3) precatalyst **4** (Figure 1)[9] which displays a long solution life and can be prepared with a broad range of phosphine ligands including bulkyphosphines. More interestingly, they can be activated under mild conditions using a weak base at room temperature to generate the desired LPd(0) species.

This Perspective outlines useful information on the recent breakthroughs performed using these G3- precatalysts during the years 2013 and 2014. The aim is to collect useful data concerning reactivity and selectivity of this promising family of precatalysts and to understand their structure and ligand–activity relationship in the C–C and C–heteroatom bonds forming reactions. For more history about preformed palladium catalysts, an excellent review was published by Colacot and co-workers in 2012.[3b]

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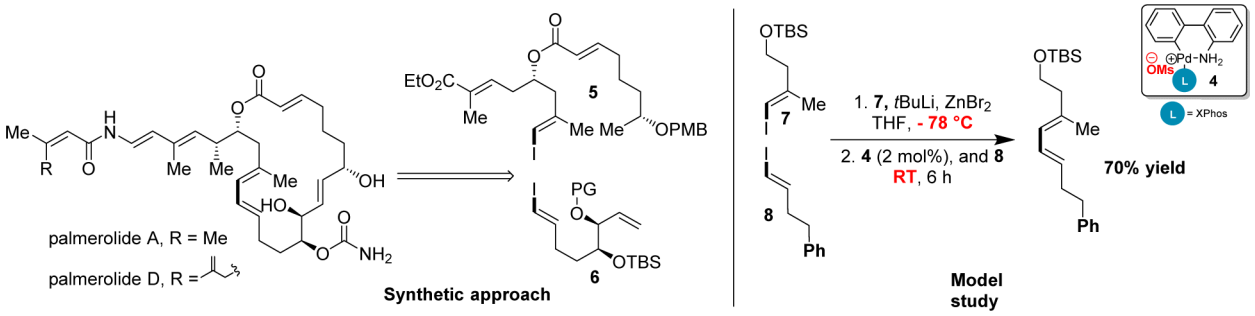
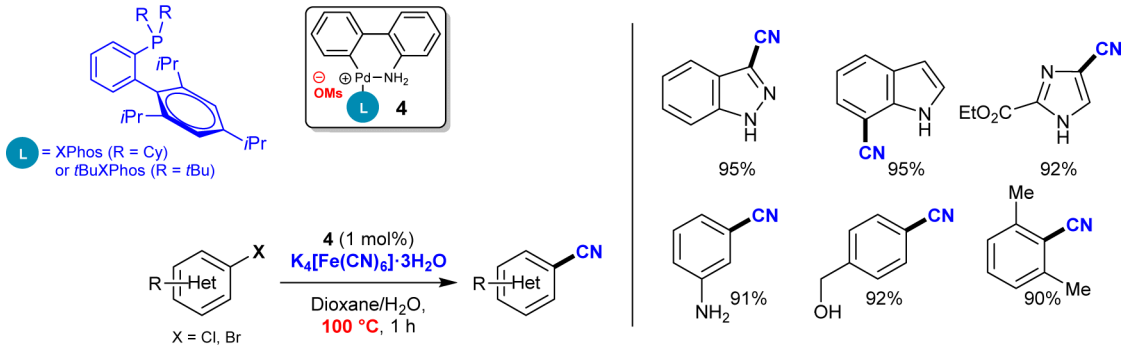
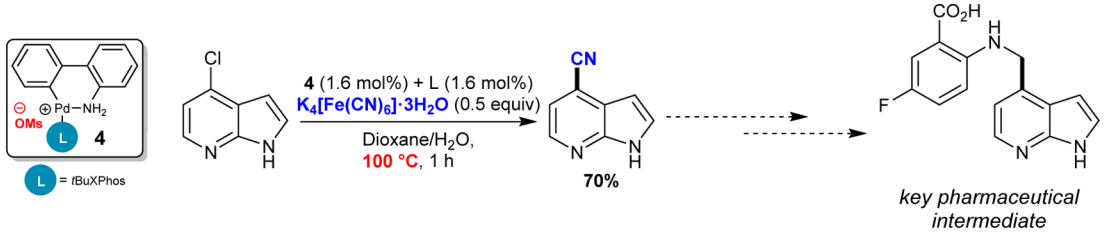
Scheme 3. Example of the Use of G3-XPhos Precatalyst in a Model Study for the Total Synthesis of Palmerolides Involving a Negishi Cross-Coupling



Scheme 4. Use of G3-XPhos Precatalyst in Cyanation of Heterocyclic Halides



Scheme 5. Application of the G3-Precatalyst to the Preparation of a Pharmaceutical Intermediate



C–C BOND FORMATION CATALYZED BY G3-PRECATALYSTS

Csp^2–Csp^2 and Csp^2–Csp Cross-Couplings. Buchwald and co-workers reported in their seminal work that the XPhos-G3 precatalyst was very efficient in Csp^2–Csp^2 Suzuki–Miyaura couplings (Scheme 2).[9] Unstable boronic acids that are extremely prone to protodeboronation, such as 2,6-difluorophenylboronic acid, could be successfully coupled with (hetero)aryl chlorides. The key success of this cross-coupling was dependent on the extremely fast activation of the XPhos precatalyst **4** at room temperature in conjunction with its high level of catalytic activity.

Very soon thereafter, the same group applied the XPhos-G3 precatalyst **4** for the Negishi coupling of challenging heteroaryl and polyfluoroaryl zinc reagents under mild conditions (Scheme 2).[10] This method is effective with a broad scope of heteroaryl halides (–I, –Br, and –Cl) and pseudohalides (–OTf). The ability of the XPhos-G3 precatalyst **4** to operate at a low catalyst concentration was examined by the group who demonstrated that the reaction proceeds with low a catalyst loading of 0.025–0.05 mol % (turnover number = 2000–4000). However, substrates bearing an ortho coordinating substituent such as an ester or a ketone usually require a catalyst loading higher than 0.1 mol % to achieve full conversion.

Among the most exciting aspects of organic chemistry in the past few decades has been the interplay between the specialized subdisciplines of organometallic chemistry and total synthesis, each enabling and advancing the other in new directions and toward greater heights. Thus, utilizing palladium precatalysts to construct complex fragments for total synthesis is highly desired. In this context, Vilarrasa and co-workers demonstrated that the G3 precatalysts can be envisioned in the total synthesis of natural products. The authors reported a nice demonstration of the use of XPhos-G3 precatalyst in their strategy approach to palmerolides via a Negishi cross-coupling (Scheme 3).[11] Although the final conditions chosen for the assembly of fragments **5** and **6** are Pd_2dba_3 (5 mol %) and XantPhos (12 mol %) at 60 °C for 16 h in their model study, XPhos-G3 precatalyst (2 mol %) allows the coupling of **7** and **8** at room temperature in a 70% yield. Performing the cross-coupling using the XantPhos-G3 precatalyst instead of Xphos-G3 may improve the yield of the coupling product in both the model study (coupling of **7** and **8**) as well as in the assembly of the fragments **5** and **6** at room temperature in the presence of lower amount of catalyst.

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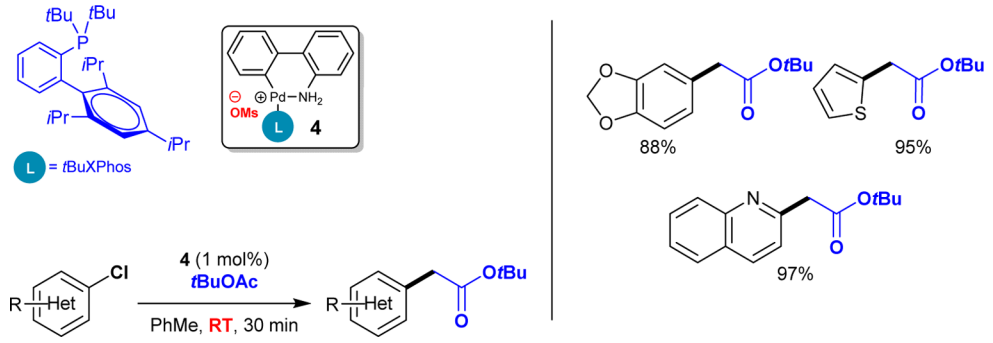
Scheme 6. Use of G3-*t*BuXPhos Precatalyst in the α-Arylation of Acetate Esters



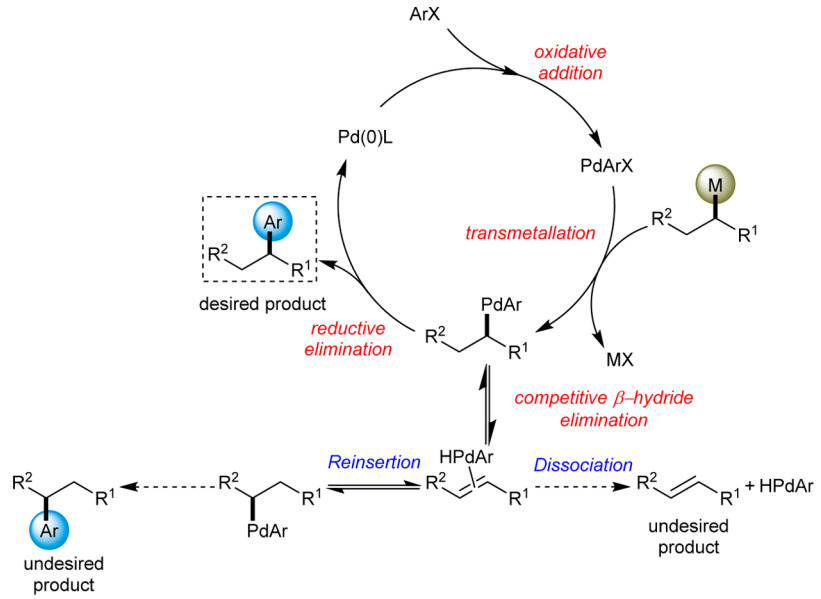
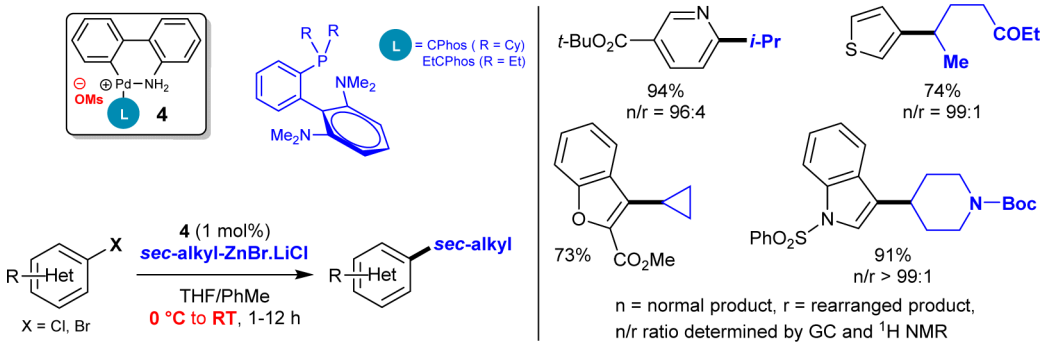


Figure 2. Possible side reactions in the Pd-catalyzed cross-coupling involving secondary alkyl nucleophiles.

Scheme 7. Use of G3-Precatalysts in Negeshi Csp^3–Csp^2 Cross-Couplings



The high efficiency of the XPhos-G3 precatalyst **4** was also highlighted in the cyanation of (hetero)aryl halides under low catalyst loading.[12] The reaction was achieved using $K_4[Fe(CN)_6]\cdot 3H_2O$, a nontoxic food additive, as a cyanide source and tolerates a wide range of functional groups (e.g., −OH, $-NH_2$, $-CO_2Et$) and N−H heterocycles, such as indazole, indole, azaindole, and imidazole (Scheme 4).

Moreover, this method was applied to the preparation of a pharmaceutical intermediate, 4-cyano-7-azaindole, which was used for the preparation of 2-[(1*H*-pyrrolo[2,3-*b*]pyridine-4-yl)methylamino]5-fluoronicotinic acid[13] (Scheme 5). The cyanation of 4-chloro-7-azaindole was performed by using 1.6 mol % of *t*-BuXPhos-G3 and an additional 1.6 mol % of *t*BuXPhos to afford the pharmaceutical intermediate 4-cyano-7-azaindole in a 70% yield.

Csp^2–Csp^3 Cross-Couplings: α-Functionalization of Carbonyl Compounds. The Pd-catalyzed α-arylation reactions of carbonyl compounds is an effective strategy to achieve the substitution of enolates,[14] often with excellent enantiomeric control.[15] However, there are very few reported examples of the selective monoarylation of enolates from acetate esters using aryl halides in which the enolate is not biased toward monoarylation. Such α-arylation reactions are typically unsuccessful as a result of the instability of alkali ester

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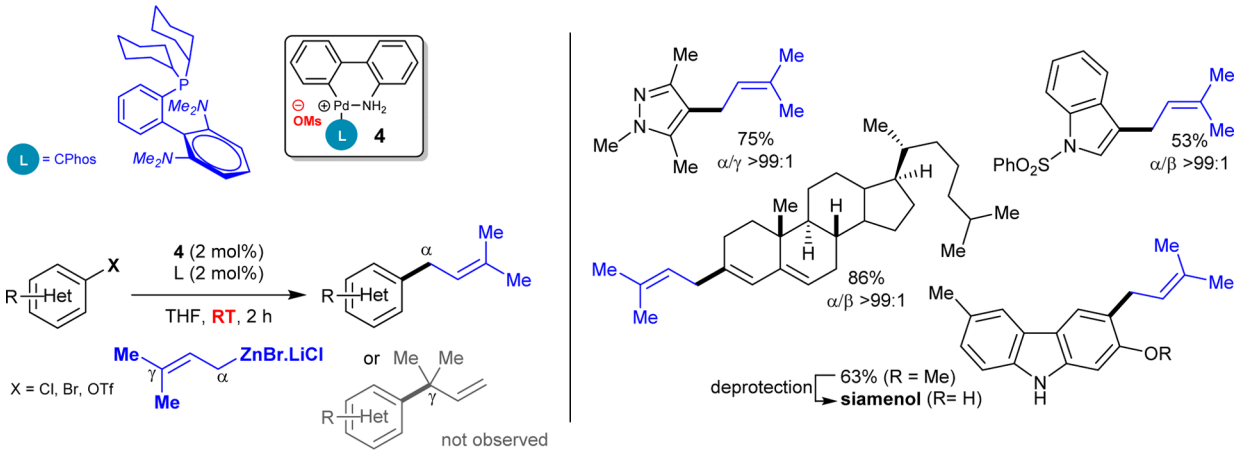
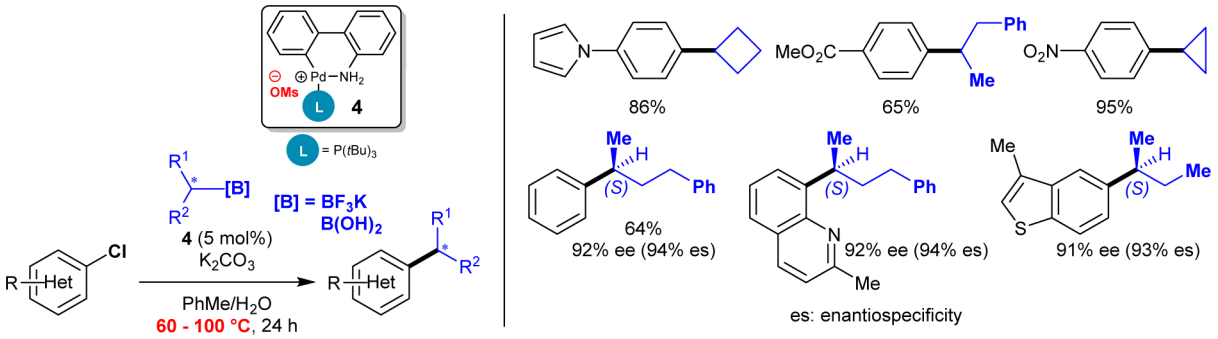
Scheme 8. Use of G3-Precatalysts in Negishi Csp^3–Csp^2 Cross-Couplings



Scheme 9. Use of G3-Precatalysts in Suzuki–Miyaura Csp^3–Csp^2 Cross-Couplings



enolates[16] or the formation of significant amounts of diarylated side products. To overcome these limitations, Buchwald and co-workers reported a simple procedure for the monoarylation of acetate esters using aryl chlorides. In the presence of *t*BuXPhos G3-precatalysts, these reactions are easily accomplished at room temperature in excellent yields employing both aryl and heteroaryl chlorides (Scheme 6).[9] Only 1 mol % of precatalyst was used for complete conversion, and no diarylated side product was observed, probably because of the use of less-reactive aryl chlorides under mild (room temperature) and fast reaction conditions.

Cross-Coupling of Csp^3–Alkyl Organometallics. The cross-coupling involving secondary Csp^3–alkyl nucleophiles remains challenging, owning to the competitive *β*-hydride elimination and migratory reinsertion that results in the formation of undesired products (Figure 2). Moreover, the transmetalation step in the coupling with secondary alkylmetal reagents is less efficient because of steric hindrance on the alkylmetal.

In 2014, Buchwald's group reported a highly selective Negishi cross-coupling of secondary alkylzinc reagents with heteroaryl halides under mild conditions (Scheme 7).[17] The development of a series of biarylphosphines bearing a 2,6-bis(dimethylamino)phenyl group proximal to the phosphine led to the identification of improved CPhos- and EtCPhos-G3 precatalysts for the coupling of electron deficient heterocyclic substrates at 0 °C to room temperature.

Furthermore, precatalyst Cphos-G3 was used successfully in a linear-selective Negishi reaction of allylzinc halides with (hetero)aryl electrophiles (Scheme 8).[18] Vinyl bromides and triflates were also converted in a complete regioselective manner into the corresponding "skipped dienes", key structural motifs found in a number of biologically active natural products. This protocol features exceptionally mild reaction conditions, broad in scope, with respect to both aryl/vinyl halide and allylzinc coupling partners. In addition, the utility of this prenylation methodology was highlighted by the synthesis of anti-HIV natural product siamenol[19] isolated from *Murraya siamensis* (Scheme 8).[20]

Very recently, the group of Biscoe and co-workers disclosed an efficient P(*t*Bu)$_3$-G3 precatalyst for the coupling of unactivated secondary alkylboronic acids as well as potassium alkyltrifluoroborate salts with aryl chlorides (Scheme 9).[21] In all cases, a >50:1 ratio of retention to isomerization products is observed during the reaction.

It is well-known that in Suzuki–Miyaura reactions,[22] both inversion[23] and retention[24] of absolute configuration have been reported for activated secondary alkylboron nucleophiles. The work of Biscoe and co-workers disclosed for the first time a enantiospecific Suzuki reaction employing an unactivated secondary alkyl boron nucleophile. Using P(*t*Bu)$_3$-G3 precatalyst, optically active potassium alkyltrifluoroborate reagents undergo efficient cross-coupling reactions with stereospecific inversion of configuration (Scheme 9).[21] The origin of the enantiospecificity of this transformation arises from the transmetalation of the secondary alkylboronic acids to Pd(II) with a clean inversion. This observation is consistent with previous reports from Aggarwal[25] and Kalbalka.[26]

C-Heteroatom Bond Formation Catalyzd by G3-Precatalysts. Synthetic organic chemists continuously pursue new reactions and chemoselective transformations under mild conditions. In this context, the catalytic formation of carbon–

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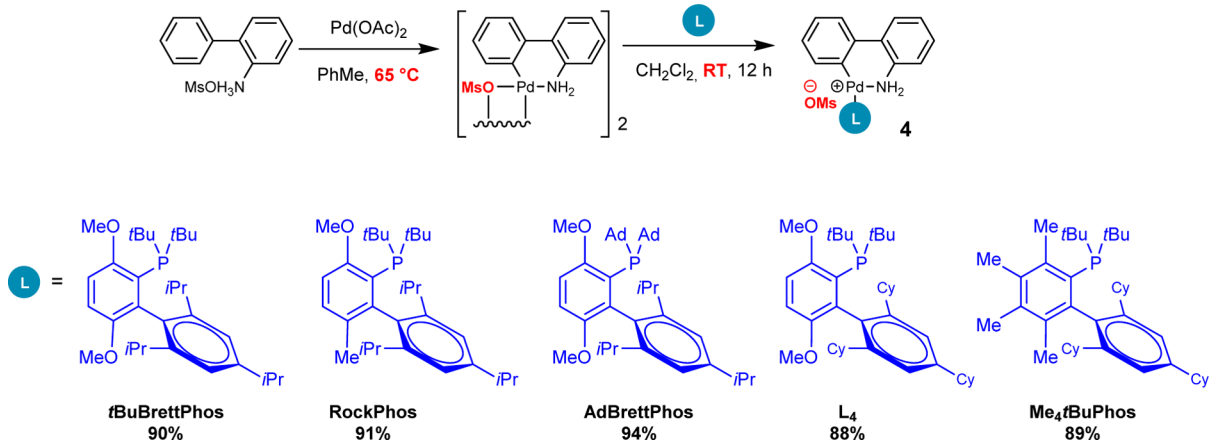
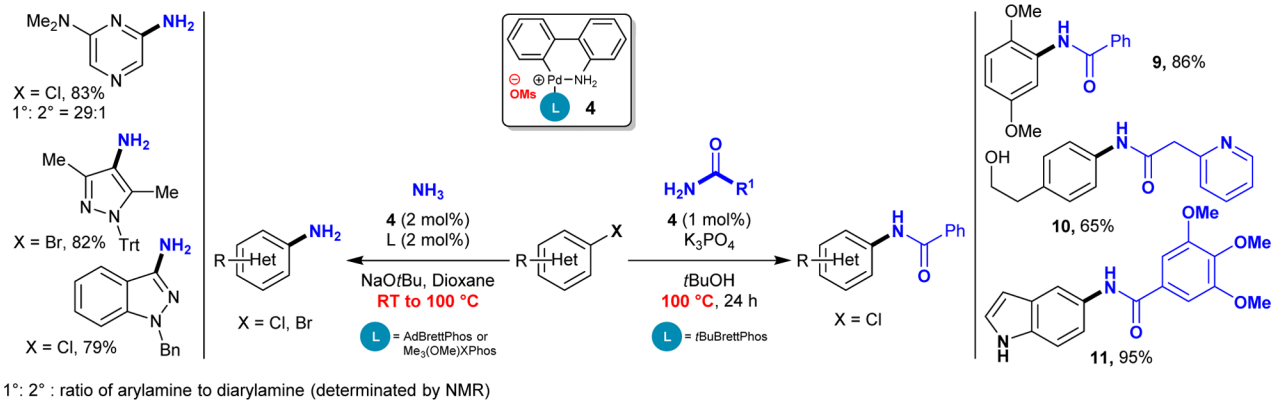
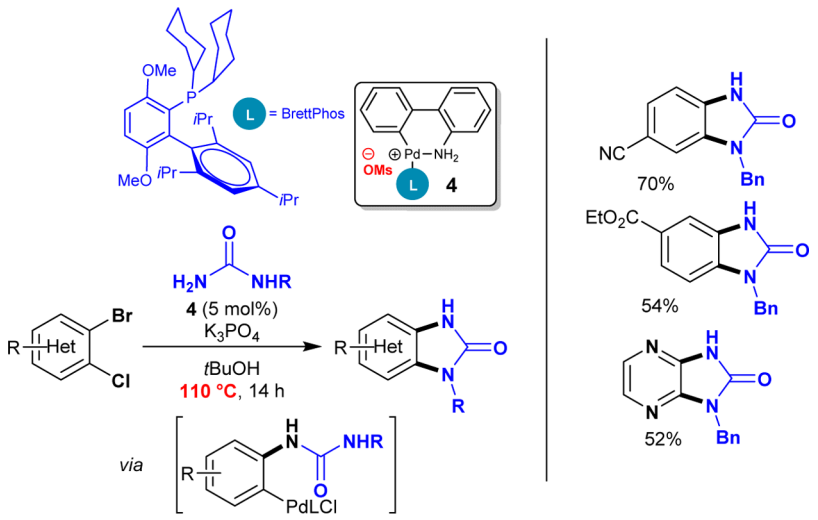
Scheme 10. Novel Series of G3 Precatalysts Bearing Bulkyphosphine Prepared Using a Revisited Protocol



Scheme 11. Use of G3-Precatalysts in the Arylation of Primary Nitrogen Nucleophiles (Amides and Ammonia)



Scheme 12. Use of G3-Precatalysts in a Regioselective Method Toward Benzimidazolones



heteroatom (N, O, S, P, etc..)[27] remains a central research focus of many research groups, and numerous studies have been devoted to the development of more general and efficient catalytic systems capable of facilitating the coupling of a diverse range of heteroatomic nucleophiles, including nitrogen (amines, amides, sulfonamides, NH-azoles, ureas, azide, etc.), oxygen (alcohols, phenols), sulfur (thiols, thiophenols), and phosphor (phosphines, phosphites) nucleophiles under mild reaction conditions.

C–N-Bond-Forming Reactions. With the aim to synthesize a large library of G3-precatalysts and to identify highly active precatalysts for the C–N bond forming reaction, Buchwald and co-workers revisited the reaction conditions for preparing a series of palladacycles of type **4**.[28] The authors found that the use of chlorinated solvents such as dichloromethane or chloroform instead of THF allowed the preparation of various G3-precatalysts **4** incorporating a large number of bulkyligand in high yields (Scheme 10).

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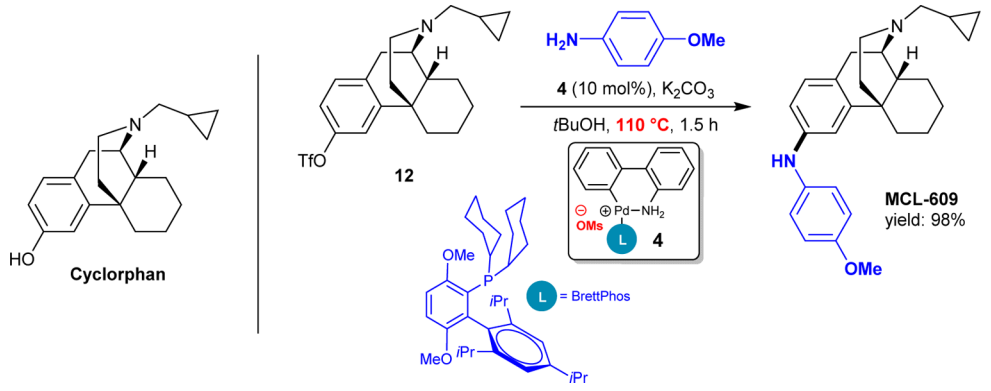
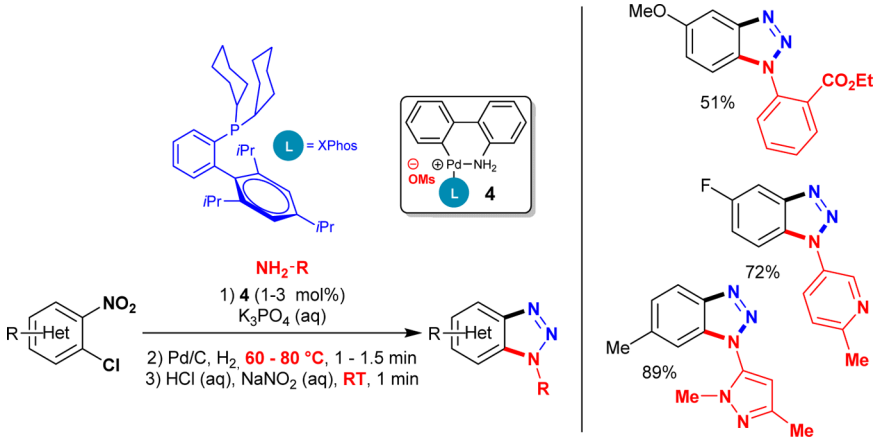
Scheme 13. Use of G3-Precatalysts in Total Synthesis of MCL-609



Scheme 14. Use of G3-Precatalysts in a Regioselective Method Toward Benzotriazoles



Among these G3-precatalysts **4**, G3-*t*BuBrettPhos displays a remarkable reactivity toward the coupling of functionalized aryl chlorides with various amides requiring only 1 mol % of palladium and a relatively short reaction time (90 min) (Scheme 11).[28] Moreover, this precatalyst displays high chemoselectivity, toward amides versus alcohol and N−H azoles. For example, no competitive C−O bond formation or N-arylation of indole in the case of products **10** and **11** was observed.[28] Just after this study, the same group reported the use of G3-precatalyst in a highly selective monoarylation of ammonia with a wide range of aryl and heteroaryl halides, including challenging heterocyclic substrates such as five-membered heterocycles and diazines (Scheme 11).[29] The authors examined the effects of biarylphosphine ligands in the selectivity of the monoarylation and showed that sterically demanding ligand, such as Me_3(OMe)XPhos or AdBrettPhos, showed high selectivity toward the monoarylation product. This selectivity can be explained by the more conformational rigidity of the biaryl backbone of these ligands as a result of the presence of the 3- and 6-methyl or methoxy groups. These effects (steric effect and rigidity) may prevent the formation of the diarylamine byproduct.

Very recently, Buchwald and co-workers realized an elegant regioselective method toward benzimidazolones via a cascade of C−N coupling of monosubstituted ureas with 1,2 dihaloaromatic systems under G3-BrettPhos catalysis (Scheme 12).[30] In this process, the heterocyclic products are formed with complete regiocontrol that stems from the chemoselective oxidative addition of the palladium catalyst to C−Br bonds in the presence of C−Cl bonds and preferential C−N bond formation of primary urea nitrogen atoms.

Neumeyer and co-workers used the same precatalyst (G3-BrettPhos) in a nice application for the synthesis of enantiomeric morphinan **MCL-609** (Scheme 13).[31] In their research program devoted to the development of opioid derivatives possessing mixed MOR and KOR activities as a treatment for cocaine abuse, the authors designed a series of opioid ligands related to Cyclorphan bearing a 3-arylamino groups such as **MCL-609**. To this end, the intermediate **12** was reacted with *p*-anisidine in the presence of 10 mol % of G3-BrettPhos and K_2CO_3 as a base in *t*BuOH at 110 °C for 1.5 h. Under these conditions, the **MCL-609** was isolated in an excellent 98% yield. Of note, when the reaction was performed using standard Buchwald−Hartwig conditions ($Pd_2(dba)_3$, dppf, sodium *tert*-butoxide, toluene, 80 °C) the yield of **MCL-609** did not exceed 13%.[32] This result clearly demonstrates again the efficiency of the G3-precatalyst, even in the modulation of complex chemical structures.

Continuous-flow processes are useful alternatives to traditional batch procedures, as has been demonstrated by both industrial and academic chemists.[33] In this content, the Buchwald group recently demonstrated the feasibility of C−N cross-coupling reactions in continuous flow[34] as well as in a multistep continuous-flow synthesis of 1-substituted benzotriazoles under consecutive multiphase reaction conditions (Scheme 14).[35] Starting from 2-chloronitrobenzene and amines, this protocol involves C−N bond formation/hydrogenation/diazotization/cyclization sequences in a regiospecific

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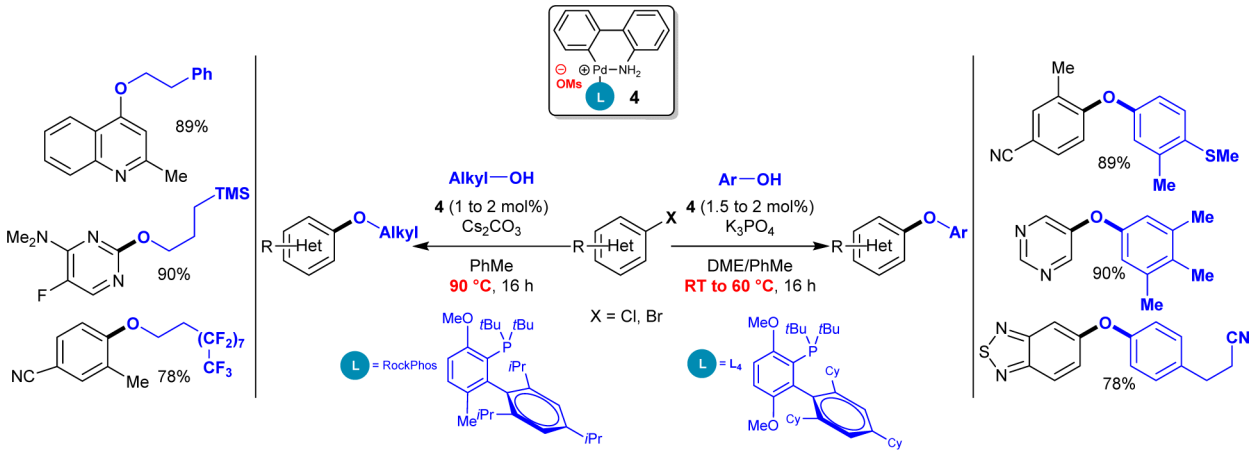
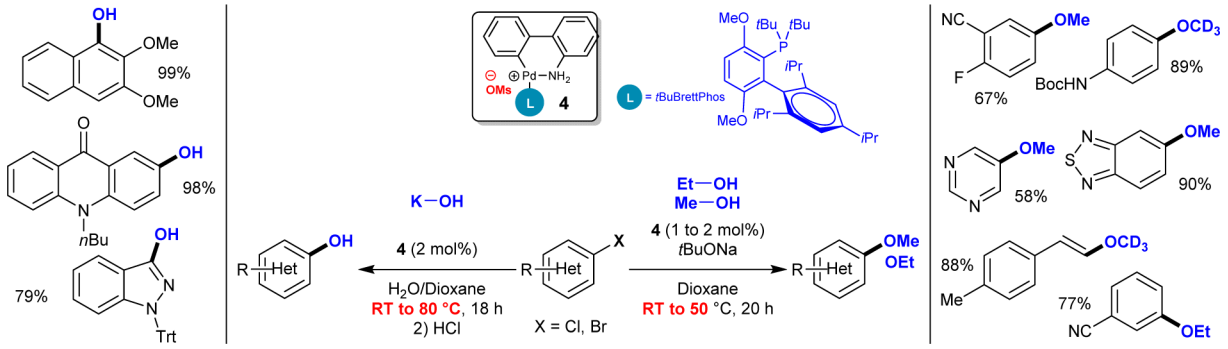
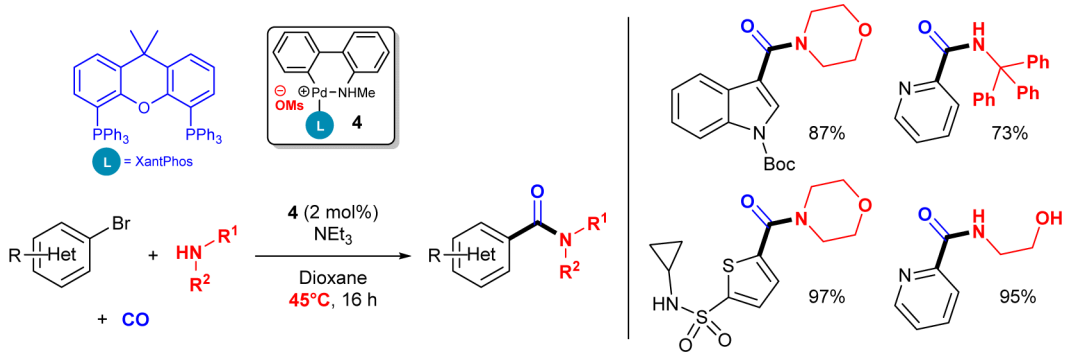
Scheme 15. Use of G3-Precatalysts in C−O-Bond-Forming Reactions



Scheme 16. Use of G3-*t*BuBrettPhos Precatalyst in C−O-Bond-Forming Reactions



Scheme 17. Use of G3-Precatalysts in Aminocarbonylation Reaction



fashion. One of the advantages of this method is avoiding the thermally sensitive diazotization reactions under batch conditions.[36] The second advantage, but not less important, is the regioselectivity of this method toward the N_1-susbtituted benzotriazoles. Most traditional methods to 1-substituted benzotriazoles suffer from a lack of selectivity, and separation of 1-, 2-, and 3-substituted benzotriazoles is oftentimes nontrivial. It is important to note that the use of the XPhos-G3 precatalyst is crucial for the success of the coupling of a 2-chloronitrobenzene substrates bearing additional electron-donating groups (Scheme 14).

C−O-Bond-Forming Reactions. Buchwald's group was also interested in assessing the performance of these new precatalysts in Pd-catalyzed C−O bond forming reactions. The authors showed that the G3-precatalyst derived from phosphine **L4** (Scheme 10) was highly efficient, allowing the formation of diarylether products in good yields and under mild reactions conditions (ambient to 60 °C, 1.5−2 mol % of Pd) (Scheme 15).[28] Similarly, when RockPhos-G3 precatalyst was used, a variety of primary alkyl alcohols bearing a β-hydrogen were coupled with aryl halides in good yields without any side product derived from β-hydride elimination.[28] The bulky phosphine RockPhos (Scheme 15) plays a critical role in promoting the reductive elimination of the LPd(aryl)(alkoxy) intermediate relative to the undesirable, competing β-hydride elimination of the alkoxy group, leading to the alkyl-aryl ethers rather than the arene side products.[37]

In light of the success of the aminobiphenyl G3 precatalysts to promote the C−O-bond-forming reaction under mild conditions, the same group disclosed an improved general method for the synthesis of a broad range of methyl arylethers by coupling methanol with a wide range of (hetero)aryl

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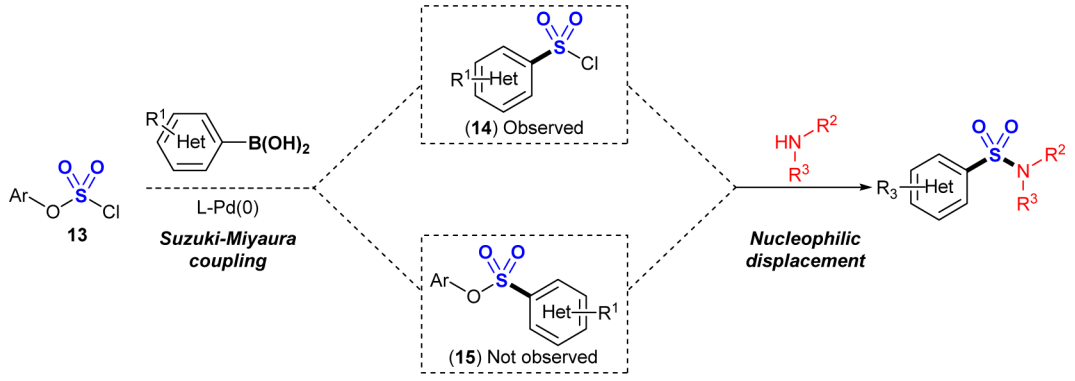
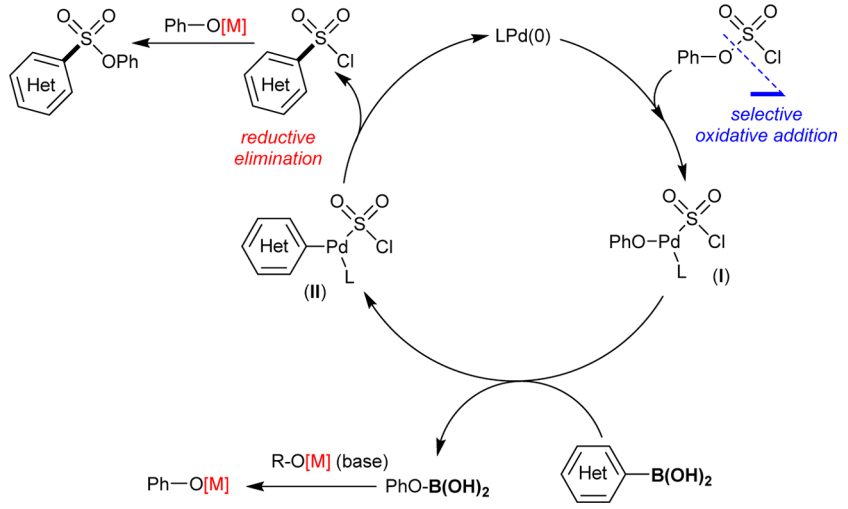
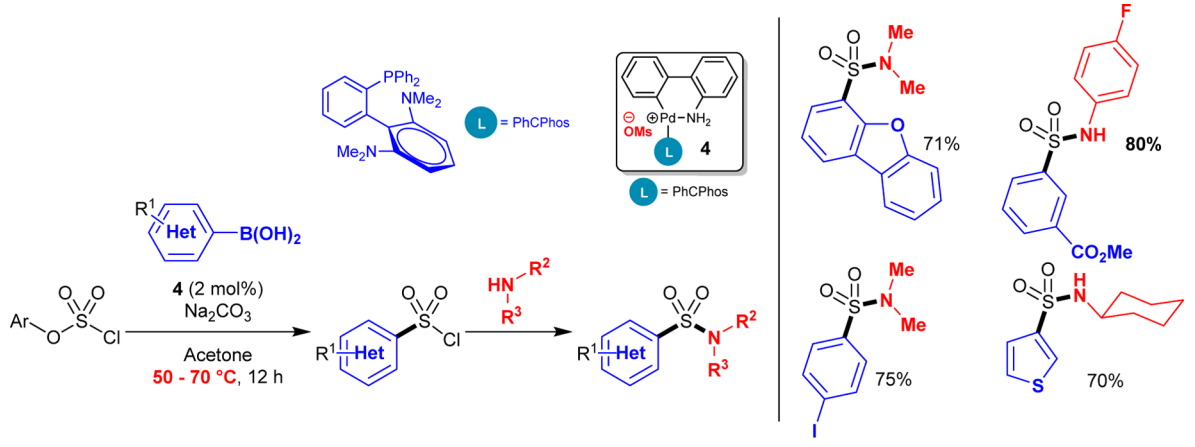
Scheme 18. Use of G3-Precatalysts in Sulfonylation of Aryl Boronic Acids



Scheme 19. Proposed Catalytic Cycle for the Sulfonylation of Aryl Boronic Acids



Scheme 20. Use of G3-Precatalysts in the Synthesis of Sulfonamides from Aryl Boronic Acids, Phenyl Chlorosulfonate, and Amines



halides.[38] Mild reaction conditions were used (rt to 50 °C) with a bulky biarylphosphine *t*BuBrettPhos-G3 precatalyst in only 1 mol % amount. The protocol also allowed the coupling of methanol-d_4 with a variety of (hetero)aryl- and vinyl halides, furnishing the corresponding trideuteriomethyl aryl and vinyl ethers (Schema 16). In addition, the authors have found that the coupling of ethanol instead of methanol proceeds under ambient conditions, affording the ethyl aryl ethers in good yields. Moreover, this catalytic system based on *t*BuBrettPhos-G3 precatalyst efficiently promotes the hydroxylation of a wide range of heteroaryl halides by using both potassium and cesium hydroxides as the "hydroxyl" source.[39]

Miscellaneous. Mild Pd-catalyzed aminocarbonylation of heteroaryl bromides with a precatalyst of type **4** was just reported (Scheme 17).[40] Skrydstrup's group in collaboration with Buchwald's group has demonstrated that the highly active XantPhos-ligated Pd species is generated cleanly and efficiently catalyzes the aminocarbonylation of a wide range of (hetero)-

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aryl bromides, with only a slight excess of CO. In this study, the authors demonstrated that the nature of the base is crucial. When a strong base, such as DBU, was employed, the yield of the desired compound decreased significantly and instead provided the double carbonylated byproduct. Triethylamine was the ideal base; when combined with XantPhos-G3, it provides efficient access to a range of products that are otherwise not easily accessible (Scheme 17).

Aryl sulfonamides were also prepared using a similar strategy. Buchwald and co-workers discovered serendipitously that coupling of aryl chlorosulfonate derivatives **13** with aryl boronic acids via a palladium catalyst generates arylsulfonyl chlorides **14** in preference to sulfonate esters **15** (Scheme 18).[41] After a fine screening of various phosphine ligands, the authors identified that the PhCPhos ligated palladacyle is a precatalyst of choice for this transformation when Na_2CO_3 is used as a base in acetone at 50 °C. Under these conditions, a number of sulfonyl chlorides were isolated in good yields. These substrates are often used as aryl halide equivalents for C−C bond forming reactions.[42]

The proposed catalytic cycle involved a chemoselective oxidative addition of highly active LPd(0) species into the SO_2−OPh bond in preference to the SO_2−Cl bond (Scheme 19). The authors postulated that the phenoxy substituent of the resulting Pd-sulfinate complex (**I**) would facilitate transmetalation without the aid of an oxygenated base.[43] After the subsequent reductive elimination from (**II**), the sulfonyl chloride was formed, accompanied by the regeneration of LPd(0) (Scheme 19).

Although most of the sulfonyl chlorides are stable to chromatography, electron-deficient compounds (e.g., $-CF_3$, $-CO_2Et$) were found to decompose to varying degrees upon attempted purification. To circumvent this problem, the authors developed a protocol in which the sulfonyl chloride intermediates were directly converted to sulfonamides by adding a primary or secondary amine to the crude reaction mixture (Scheme 20).

Weakly nucleophilic anilines may also be incorporated into the sulfonamide moiety, but pyridine is required to facilitate amination in this case. This reaction tolerated a wide range of functional groups, excellent site selectivity, and orthogonal reactivity toward other reactive functions, such as the carbon−iodine bond. In this case, Pd(0) reacts with phenyl chlorosulfinate in preference to aryl iodide groups bearing electron-withdrawing sulfonyl groups para to the iodo substituents (Scheme 20).

CONCLUSION

In conclusion, with the advent of the third generation of precatalysts **4** by Buchwald's group, various challenging C−C coupling and C−heteroatom bond formations under extremely mild conditions have now been achieved. These advances in catalysis undeniably open new perspectives in Pd-catalyzed cross couplings at room temperature. We believe that subsequent developments in the field of catalysis, such as C−H activation as well as C−S- and C−P-bond-forming reactions, will be addressed using this generation of precatalysts.

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Notes

The authors declare no competing financial interest.

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