Catalysis
PEPPSI™ Catalyst

General Background
Advantages of PEPPSI™
Reaction Types
- Negishi
- Suzuki
- Buchwald–Hartwig
- Kumada
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General Background

Palladium has played a central role in the expeditious preparation of complex organic molecules, since the discovery and subsequent catalytic use of \( \text{Pd(PPh}_3\text{)}_4 \) by Malatesta, Anoletta and others.\(^1\) In the world of catalysis, the ancillary ligands of any Pd complex represent the chassis, whereas the Pd center functions as the driver for cross-coupling reactions. These metal-catalyzed processes arguably remain the most powerful means to generate C–C, C–O, and C–N bonds in the synthetic chemist's toolbox.\(^2,3\) Catalyst developments in the cross-coupling field have been concentrated in rapid design and deployment of complexes containing tertiary phosphine ligands. The disadvantages of utilizing phosphines as ligands for Pd are numerous, including their high expense, sensitivity, and lack of commercial sources for late generation compounds. Perhaps most importantly, few catalysts exhibit superior activity among broad substrate classes and reaction paradigms. It should also be noted that Pd(PPh\(_3\))\(_4\) is widely applied in catalysis, but this complex suffers from poor stability upon storage as well as advised handling under nitrogen.

\(N\)-Heterocyclic carbene (NHC) Pd complexes have been designed in order to overcome some of these limitations.\(^4\) Professor Mike Organ at York University, along with co-workers Dr. Chris O'Brien and Dr. Eric Kachetche, have developed an elegant Pd–NHC catalyst system built around a simple concept.\(^5\) They reacted PdCl\(_2\), with a bulky NHC ligand, 2,6-diisopropylphenylimidazolium chloride (IPr), and a \(\sigma\)-donating 3-chloropyridine ligand for stability. The title complex, PEPPSI\(^\text{™}\), stands for Pyridine-Enhanced Precatalyst Preparation Stabilization and Initiation. The 3-chloropyridyl ligand functions as a ‘throw-away’ ligand, while the bulky IPr ligand improves reductive elimination of the substrate that in turn increases TONs (Figure 1).\(^6\) The \(\sigma\)-donating power of the NHC ligand also binds the metal more tightly than traditional phosphines and thus prevents metal dissociation. The character of the NHC ligand (unsaturated vs. saturated) does not affect catalyst activity, but does affect catalyst robustness and ease of formation.

Sigma-Aldrich is proud to offer gram-scale quantities of the PEPPSI\(^\text{™}\)-IPr catalyst in our collaboration with the Organ research group. The efficient mediation of C–C and C–N bond-forming processes, robust stability, and competitive pricing make it attractive for widespread application in the research and fine-chemical arena. For a complete listing of products related to your specific research efforts, “Please Bother Us” at amaestri@sial.com. We welcome your inquiries and look forward to accelerating your research success.

Figure 1

\(\text{IPr ligand enables high catalyst performance}\)

\(\text{Pyridyl ligand provides added stability and creates a well-defined catalyst structure}\)

About Our Cover

The cover illustration shows a rendering of the PEPPSI\(^\text{™}\)-IPr catalyst X-ray structure. The 3-chloropyridine ligand bisects the N-heterocyclic carbene (NHC) ligand and lies roughly in the same plane as the ancillary chloride ligands, effectively granting the expected square planar geometry about the Pd(II) metal center. Please note that the hydrogens on the 2,6-isopropylphenyl–NHC and pyridyl ligands have been omitted for clarity.
Representative Example with PEPPSI™

Scheme 1 illustrates the strong ability of PEPPSI™ to effect cross-couplings (sp²–sp² Negishi) under mild reaction conditions. The aryl bromide was completely converted to 4-methyl-4’-methoxy-biphenyl in 2 h at room temperature, whereas competitive Pd systems require overnight reaction times to reach adequate conversions. Another compelling feature of the PEPPSI™ system is the low (1 mol %) loadings in Negishi couplings, wherein sp³–sp³ couplings have been achieved in short (30 min) reaction times with high conversions. Previous NHC protocols involving alkyl–alkyl coupling reactions have not been accomplished successfully in high yield.

PEPPSI™ Activation and Catalytic Cycle

The challenges associated with improving palladium catalyst systems for cross-coupling are often related to the rate of active catalyst formation and subsequent stability throughout the catalytic cycle. In the case of PEPPSI™–IPr, rapid, quantitative conversion to product in Negishi couplings has been documented by the Organ group. In this catalyst system, activation most likely occurs via reduction of the Pd(II) center by the organometallic reagent, followed by pyridine dissociation from the newly formed Pd(0) species (Scheme 2). The yield of n-heptylbenzene under typical Negishi cross-coupling conditions is strongly dependent upon the structural environment around the Pd center. Isopropyl groups influence the conversion of cross-coupling product, which may imply a stabilizing influence on the PEPPSI™–IPr Pd(0) center versus NHC analogs 1a and 1b (Table 1). Thus, the bulky isopropyl NHC ligand accelerates the reductive elimination of n-heptylbenzene, while stabilizing the Pd center.

(1,3-Diisopropylimidazol-2-ylidene)(3-chloropyridyl)palladium(II) dichloride

**C₃₂H₄₁Cl₃N₃Pd**

MW: 679.46

<table>
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**Table 1**

General Background

<table>
<thead>
<tr>
<th>entry</th>
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<th>yield of n-heptylbenzene</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>ZnBr</td>
<td>100% (1), 34% (1a), 8.0% (1b)</td>
</tr>
<tr>
<td>2</td>
<td>BBu₂</td>
<td>100% (1), 31% (1a), 6.5% (1b)</td>
</tr>
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**Scheme 1**

**Scheme 2**
Advantages of the PEPPSI™–IPr Catalyst

- Extremely stable to air and moisture
- Commercialized on kilo scale
- Improved or comparable activity to known Pd catalysts
- High performance in various reaction paradigms
- Many reactions occur at room temperature
- No need for additional ligands ➞ one-component catalyst
- Competitive pricing

Stability and Handling

Unlike traditional palladium phosphine and NHC catalysts, PEPPSI™ is robust and can be stored indefinitely outside an inert atmosphere. The catalyst may be weighed out on bench utilizing normal methods and can even be subjected to a water workup without observable decomposition by 1H NMR. Perhaps most impressively, PEPPSI™ has been heated in dimethylsulfoxide at 120 °C for hours without decomposition and subsequent deactivation of the catalyst. This Pd(II) complex becomes active in situ through reduction to the Pd(0)–NHC active catalyst—thus it can be considered a ligand stabilized Pd(PPh₃)₄ alternative, minus the handling deficiencies. The picture above brilliantly illustrates the multi-gram synthesis and impressive stability of PEPPSI™–IPr in a coffee mug under atmospheric conditions!

Reaction Types

- Negishi Reactions
- Suzuki Reactions
- Buchwald–Hartwig Aminations
- Combined Amination/Heck Reaction
- Kumada Couplings
- Future Cross-Couplings

Negishi Couplings

Negishi reactions are comprised of the coupling between an alkyl halide with an alkyl organometallic reagent, which is unexplored territory for Pd–NHC complexes. The Organ group has achieved these difficult transformations with PEPPSI™–IPr and in the process has developed a general, efficient protocol with broad functional group tolerance. This PEPPSI™ catalyst satisfies two main criteria required for successful couplings: 1) the reaction should be conveniently run without the need for special handling, i.e., use of a glove box; 2) the catalyst system must be extended to a diverse spectrum of reaction partners.

The success of this Pd–NHC catalyst system is highly dependent upon the activation of the Pd(0) catalyst, in part through the use of LiCl/Br as an additive. The Organ group attempted to perform a Negishi cross-coupling of n-butylzinc, as prepared by Hou and co-workers, with the requisite bromoalkane and only recovered starting material after stirring the reaction for hours at room temperature. They applied the same reaction conditions, but used n-butylzinc bromide prepared from the method of Hou along with 2 eq. of LiBr and found that the reaction produced the sp³–sp³ coupled organic in excellent yield in 30 min. Thus, the activation of the alkylzinc reagent, via the formation (presumed) of a lithium zincate, is an important driving force for the successful utilization of the PEPPSI™ catalyst in Negishi couplings.

**PEPPSI™–IPr Loading**

The Negishi reaction conditions utilizing PEPPSI™ have been optimized and are presented in Table 2. Note that catalyst loadings as low as 0.5 mol % show complete conversion to n-heptylbenzene within 3 h at room temperature.

**PEPPSI™–IPr vs. in situ**

The Organ group ran a direct comparison of PEPPSI™ versus an in situ generated NHC complex and found that the former system gave apparent TON h⁻¹ of 300 at 0.1 mol % loading, while the latter

<table>
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<tr>
<th>Entry</th>
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<th>Yield (%)</th>
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<tr>
<td>5</td>
<td>0.1</td>
<td>63</td>
</tr>
<tr>
<td>6</td>
<td>1, 15 min</td>
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</table>

Table 2

![Figure 2](image-url)
system afforded only 7.5 TON h⁻¹ at 4 mol % loading (Figure 2). It should be mentioned that it was not practical to measure the reaction rate of the isolated PEPPSI™ catalyst utilized in a coupling reaction at a loading of 1 mol %, because the rates were extremely fast. This comparison shows that only ca. 0.1 mol % of an active catalyst is formed at 1 h reaction time, even though 4 mol % of the precursors are used, when considering the apparent TONs and assuming that the same active species is generated in both cases. This finding clearly proves the superiority of the preformed PEPPSI™ catalyst over the in situ methodology.

Organohalide Compatibility in the Negishi Reaction
Alkyl chlorides and sulfonates have effectively been coupled by adding 2 eq. of LiBr to the reaction mixture. Interestingly, alkyl chlorides and mesylates required a THF/NMP or THF/DMI ratio of 1:3 to achieve high product yields, whereas the corresponding alkyl bromides were coupled in high yields utilizing a solvent ratio of 2:1 (THF/NMP). These observations present the rare opportunity to selectively couple an alkyl bromide in the presence of an alkyl chloride, followed by an alkyl chloride coupling in a sequential fashion. Table 3 illustrates the effectiveness of the PEPPSI™ catalyst system, wherein the cross-coupling of organochlorides and bromides, aryl triflates, and alkyl mesylates runs smoothly in all possible pairings. Catalyst 1 offers the widest substrate range performed successively in the Negishi reaction.

Experimental Conditions
Alkyl halide (1 eq.), alkylzinc bromide/chloride (1.6 eq.), PEPPSI™–IPr (1 mol %), THF/NMP or THF/DMI, room temperature to 60 °C. For all Negishi couplings the following workup procedure was used: after reaction completion, the solution was diluted with ether (~5 x volume) and washed successively with a 1 M Na₂EDTA solution (3 eq. of NaOH with EDTA), water, and brine. The combined organic solution was dried with MgSO₄, filtered through a sintered funnel, the solvent removed in vacuo, and the residue purified by flash chromatography.

Representative Experimental Procedures and Results
Negishi Substrate Scope: sp³–sp³ couplings
sp³–sp³ couplings, Scheme 3: a scintal vial was charged with 1 (0.034 g, 1 mol %) and a stir bar in air. Under an inert atmosphere LiBr (0.139 g, 0.8 mmol) was added followed by a septum. The vial was purged with argon after which THF (0.8 mL) and DMI (0.8 mL) or NMP (0.8 mL) were added and the mixture stirred until the solids dissolved. After this time, the organozinc (0.8 mL, 1 M in DMI or NMP, 0.8 mmol) and the organohalide or pseudohalide (0.5 mmol) were added. The septum was replaced with a Teflon®-lined cap under a N₂ flow and the reaction stirred for 2 h, followed by workup (cf. above).

PEPPSI™–IPr (1) is a highly efficient and mild catalyst for forming alkyl-alkyl bonds, as illustrated in Figure 3. Sp³RX–sp³RZnX couplings mediated by 1 include a wide spectrum of functionality such as esters, nitriles, and amides (2–5). Notably the terminal alkynyl TMS group in compound 7 is completely stable to the cross-coupling of an alkyl chloride under room temperature reaction conditions. These results lend credence to the possibility of coupling substrates that contain biologically active components and subsequent expeditious synthesis of natural product intermediates. The wide range of alkyl bromides, chlorides, and tosylates supported by the PEPPSI™ system extend the general usefulness (compounds 2–7) of this reaction paradigm. Incredibly, the Organ research group successfully achieved the coupling of a bromide in the presence of a chloride by judicious choice of reaction conditions (compound 2).

For all Negishi couplings the following workup procedure was

<table>
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<tr>
<th>Entry</th>
<th>R¹</th>
<th>X</th>
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<td>71</td>
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^a GC yield against calibrated undecane internal standard performed in duplicate. ^b THF/DMI, 2:1. ^c THF:DMI, 1:3. ^d THF:DMI, 1:2. ^e THF:NMP, 2:1, no LiCl/Br.

Table 3

![Scheme 3](image-url)

![Scheme 4](image-url)

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Negishi Substrate Scope: $sp^1$–$sp^2$ couplings

$sp^1$–$sp^2$ couplings, Scheme 4: A vial was charged with 1 (0.034 g, 1 mol %) in the air and then ZnCl$_2$ (0.107 g, 0.8 mmol) and a stir bar were added. The vial was capped with a rubber septum and then purged with argon. THF (0.8 mL) was added along with the required Grignard-type reagent (0.8 mL, 1.0 M in THF; 0.8 mmol) and the mixture stirred until a white precipitate formed. Under an N$_2$ atmosphere, LiBr (0.139 g, 1.6 mmol), DMI (0.8 mL), or NMP (0.8 mL), and the organohalide or pseudohalide (0.5 mmol) were added. The septum was replaced with a Teflon®-lined cap under a N$_2$ flow and the reaction stirred for 2 h, followed by workup conditions (cf. above).

The range of substrates successively applied in the Negishi reaction for $sp^1$($RX$)–$sp^2$($R$ZnX) couplings includes both electron-donating and -withdrawing substituents on the arylic reaction partner (Figure 4). Note the coupling of chiral (S)-citronellyl bromide, in which the final product shows no observable erosion of enantiopurity (compound 8). The mild nature of the PEPPSI™ catalyst tolerates pendant alkenyl and alkynyl functional groups as well as the often sensitive TMS group (8–10). Isolated product yields in this coupling class are all greater than 80%.

Negishi Substrate Scope: $sp^2$–$sp^2$ couplings

$sp^2$–$sp^2$ couplings, Scheme 5: A scintal vial was charged with 1 (0.034 g, 1 mol %) and a stir bar in air. Under an inert atmosphere, LiBr (0.139 g, 0.8 mmol) was added followed by a septum. The vial was purged with argon after which THF (0.8 mL) and DMI (0.8 mL) or NMP (0.8 mL) were added and the mixture stirred until the solids dissolved. After this time, the organozinc (0.8 mL, 1.0 M in DMI or NMP, 0.8 mmol) and the organohalide or pseudo halide (0.5 mmol) were added. The septum was replaced with a Teflon®-lined cap under a N$_2$ flow and the reaction stirred for 2 h, followed by workup (cf. above).

PEPPSI™–IPr complex 1 is able to catalyze the coupling of aryl halides (or triflates) with alkylzinc reagents in high yield (Figure 5). Furthermore, all reactions studied displayed no obvious transmetallation to form arylic reagents. The mildness of the PEPPSI™ system extends to the Negishi coupling of a chiral zinc reagent with an acyl chloride (14), wherein subsequent decarbonylation was not observed under the reaction conditions. Also heteroatom-containing substrates were carried forward with 100% fidelity, further demonstrating the benefits of this catalyst system to the synthetic community.

Negishi Substrate Scope: $sp^2$–$sp^3$ couplings

$sp^2$–$sp^3$ couplings, Scheme 6: A vial was charged with 1 (0.034 g, 1 mol %) in the air and then ZnCl$_2$ (0.107 g, 0.8 mmol) and a stir bar were added under an inert atmosphere. The vial was capped with a rubber septum and then purged with argon. THF (0.8 mL) was added along with the required Grignard-type reagent (0.8 mL, 1.0 M in THF; 0.8 mmol) and the mixture stirred until a white precipitate formed (ca. 15 min). Under an inert atmosphere, NMP (0.8 mL) and the organohalide or pseudohalide (0.5 mmol) were added. The septum was replaced with a Teflon®-lined cap under a N$_2$ flow and the reaction stirred for 2 h, followed by workup under the conditions described above.

The high activity of PEPPSI™ catalyst 1 in Negishi couplings offers a distinct advantage for C–C bond-forming reactions in homogeneous catalysis. To this end, 1 holds great promise as a generally applicable catalyst for a wide variety of cross-coupling paradigms. The $sp^2$–$sp^2$ couplings shown represent direct access to sterically hindered biaryls and heteroaromatic systems utilized as drug platforms in natural product synthesis (Figure 6). A diverse spectrum of electron-donating and -withdrawing partners utilized in these $sp^2$–$sp^2$ couplings solidifies PEPPSI™’s claim as a more active catalyst in Negishi processes than related and well-studied Pd-phosphine systems.
PEPPSI™–IPr Advantages in the Negishi Coupling

- No glove-box handling required
- Prototypical and advanced couplings possible
- Reactions performed at room temperature in a few hours
- Selectively activate a bromide over a chloride
- Diverse range of halides: Cl, Br, I, OTs, OMs, or OTf

Suzuki Couplings

Suzuki reactions involve the coupling of organoboron partners with alkyl, aryl, and alkenyl halides or triflates (Scheme 7). PEPPSI™ can be used effectively with a wide range of electron-rich ( deactivated) and electron-poor (activated) substrates. The high activity of this catalyst system allows for the facile, rapid production of a wide array of drug intermediates, heteroaromatics, and bulky organic building blocks in high isolated yields (Figure 7, all via Method A).

Different procedures were utilized (Methods A–D, cf. below) that enabled the Organ group to expand the protocol to include potassium trifluoroborates by running the reaction in methanol. The flexibility of this catalyst system allows for the facile, rapid production of a complex array of organic building blocks in high isolated yields (Figure 7, all via Method A).

Representative Experimental Procedures and Results

Procedure for Method A:
A vial was charged with potassium tert-butoxide (0.154 g, 1.30 mmol) and complex 1 (0.0068 g, 0.01 mmol) in the air, followed by purging with argon in triplicate. Tech grade isopropyl alcohol, 1.0 mL, was added via syringe and the solution was stirred at room temperature until a color change from yellow to red/brown was observed (ca. 10 min). The boronic acid (1.20 mmol) was added under an argon flow, the vial was then resealed followed by the organohalide (1.00 mmol) being added via syringe. The reaction was stirred at room temperature for the indicated time period and then diluted with diethyl ether (2 mL). After two additional 2-mL washings, the organic solution was dried with MgSO4, filtered, concentrated, and purified by flash chromatography.

Procedure for Method B:
A vial was charged with complex 1 (0.0068 g, 0.01 mmol) in the air, K2CO3 (0.207 g, 1.50 mmol), the potassium trifluoroborate (0.55 mmol), and the organohalide (0.5 mmol) by running the reaction in methanol. The solution was stirred at 60 ºC for the specified time period, followed by dilution with diethyl ether (2 mL). After two additional 2-mL Et2O washings, the organic solution was dried with MgSO4, filtered, concentrated, and purified by flash chromatography.

Procedure for Method C:
A vial was charged with complex 1 (0.0068 g, 0.01 mmol) in the air, K2CO3 (0.207 g, 1.50 mmol), the potassium trifluoroborate (0.55 mmol), and the organohalide (0.5 mmol), followed by sealing with a septum and purging with argon in triplicate. Tech grade methanol, 2.0 mL, was added and the solution stirred at 60 ºC for the specified time period, followed by dilution with diethyl ether (2 mL). After two additional 2-mL Et2O washings, the organic solution was dried with MgSO4, filtered, concentrated, and purified by flash chromatography.

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Procedure for Method D:
Solid KOH (0.84 g, 1.50 mmol) was utilized instead of solid K$_2$CO$_3$; otherwise Method B was utilized and the reaction carried forward at room temperature instead of 60 °C.

**PEPPSI™-IPr Advantages in the Suzuki Coupling**
- No glove-box handling
- Boronic acids and trifluoroborates well tolerated
- The halide can be Cl or Br
- Strong and mild bases have been applied successively
- Base sensitive substrates are acceptable

**Buchwald–Hartwig Aminations**
Since the work of Buchwald and others, palladium-catalyzed C–N bond-forming methodologies have traditionally focused on the use of (mostly) bulky, electron-rich phosphines as the ancillary ligands of choice. The Organ group was pleased to discover that PEPPSI™-IPr is an excellent catalyst for the palladium-catalyzed cross-coupling of aryl chlorides and bromides with amines. The results in Figure 9 indicate that use of this catalyst system allows for the successful arylation of various amines with superb yields. Morpholine, amines, and even adamantylamine undergo facile amination to afford a variety of aryl- and biazylenes. It is worth noting that the mild reaction conditions (temp. and base) tolerate electron-rich, electron-poor, and heteroaromatic substrates. This finding also shows that Pd–NHC complexes are not only viable as catalysts, but in many cases manifest tremendous efficiency and atom-economy in aromatic C–N bond-forming processes.

A new mild protocol expands the scope of homogeneous Pd C–N bond-forming catalysis even further. The indole moiety is one important element in organic compounds that exhibits pharmacological activity. The most popular method utilized for indole synthesis is the Fischer indole synthesis, wherein an N-acetyl hydrazine is transformed into the indole architecture through a sigmatropic rearrangement. As a complement to that well-known methodology, the Organ group has reacted a vinyl halide with various 2-bromoanilines in the presence of PEPPSI™ to afford 2-substituted indoles in good yields. This elegant strategy is being applied toward the expedious preparation of 2-alkyl and 2-aryl indoles for combinatorial libraries.

**Kumada Couplings**
Many studies have been performed on the oxidative addition of aryl halides with Pd(0) and subsequent coupling of Grignard reagents. However, deficiencies in these previous examples include high catalyst loadings, high temperatures, and the necessity of aryl iodide substrates to reach adequate conversions. The Organ group has reported Kumada couplings of various aryl chlorides with Grignard reagents (Figure 11). These room-temperature oxidative additions of aryl chlorides equal the best results to date. Reactions with 1–2 mol % PEPPSI™-IPr in THF/DME (1:1) at room temperature produced the respective biaryl organics in excellent yields.

Note that both electron-rich and electron-poor Grignard reagents underwent reaction as well as sterically hindered aryl chlorides. This mild Kumada protocol shows superior tolerance of ether, TMS, and alkynyl functionalities. Heteroaromatic substrates undergo Kumada couplings in good yields at room-temperature and with low catalyst loadings (Scheme 10). Furthermore, functionalized 5-aryl-substituted indoles are produced in good yields (Scheme 11). The results shown in Figure 11 present a strong case for the wide acceptance of the PEPPSI™ catalyst for new discoveries in Kumada-type cross-couplings.

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**Figure 9**

**Figure 10**

**Figure 11**

**Scheme 10**

**Scheme 11**
Future Generation PEPPSI™

During the past decade, progress has been achieved in developing palladium-catalyzed cross-coupling reactions of arylsilanes with organic halides, referred to in the literature as the Hiayama coupling.16 Perhaps not surprisingly, organosilicon compounds are attractive substrates in synthetic chemistry due to their ease of handling and (often) low toxicity. Most Pd-catalyzed Hiayama couplings have focused on Csp²–X electrophiles, although a report from Fu and co-workers describes a highly active Pd catalyst system effective at coupling alkyl bromides in good yields (Scheme 12).17 Interestingly, Fu reports that the combination of PdBr₂ and 2,6-dimesitylphenylimidazolium chloride (IMes) produces an active catalyst utilized in the direct arylation of alkyl bromides. Based upon the excellent achievements of the PEPPSI™–IPr catalyst covered herein, the Organ research group intends to begin exploring related Hiayama cross-coupling reactions of unactivated alkyl halides with organosilicon compounds.

Palladium-catalyzed allylic substitution reactions are another attractive paradigm for the formation of carbon–carbon bonds in synthetic chemistry. The viability of PEPPSI™–IPr to facilitate these transformations will be assessed by the York University research group and overall TONs. The Organ group is prepared to explore new reaction paradigms with the PEPPSI™–IPr catalyst in order to maximize its potential in industrial applications. Future PEPPSI™ catalysts are forthcoming, including complexes that have been modified in a unique fashion, while accelerating the rate of reductive elimination and overall TONs. The Organ group is prepared to explore new reaction paradigms with the PEPPSI™–IPr catalyst in order to maximize its potential in industrial applications. Future PEPPSI™ catalysts are forthcoming, including complexes that have been modified in the metal coordination sphere and/or the NHC architecture.

Presently, the PEPPSI™ catalyst system provides effective demonstrations of sp³–sp¹, sp³–sp², and sp²–sp² couplings of various types covering Negishi, Suzuki, and Kumada reactions. The impressive reactivity and practical nature of PEPPSI™ empowers the research chemist with the ability to mediate transformations that are directly applicable to natural product synthesis and bulk chemical production on industrial scale. The key features of PEPPSI™–IPr include the air-stability of the precatalyst and its ready activation into the catalytic cycle. Upon reduction to Pd(0), the IPr–NHC ligand stabilizes the metal center in a unique fashion, while accelerating the rate of reductive elimination and overall TONs. The Organ group is prepared to explore new reaction paradigms with the PEPPSI™–IPr catalyst in order to maximize its potential in industrial applications. Future PEPPSI™ catalysts are forthcoming, including complexes that have been modified in the metal coordination sphere and/or the NHC architecture.

References


(11) Organ, M. G. et al. manuscript in preparation.


(15) Organ, M. G. et al. manuscript in preparation.


Sigma-Aldrich, in collaboration with Rieke®, is proud to offer a variety of organozinc reagents in research-scale quantities.

Organozinc reagents have been utilized in numerous cross-coupling paradigms, as illustrated by abundant research publications in the catalysis field. Heteroaromatics, fluorinated aryls, and electronically diverse organozincs have been combined with alkyl- and arylhalides to form cross-coupled adducts in excellent yields.

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MacMillan and co-workers have created chiral imidazolidinone organo-catalysts that function as the linchpin in a variety of directed enantioselective organic reactions, including the enamine-catalyzed α-chlorination and 1,3-dipolar cycloaddition of aldehydes. Sigma-Aldrich is pleased to offer six imidazolidinone organocatalysts in our collaboration with Materia, Inc. that mediate rapid and enantiocontrolled C–F and C–H bond formation. In the former process, catalyst 1 was utilized in low (5 mol %) loadings in the first example of organocatalytic advanced enantioselective α-fluorination of aldehydes to afford a broad spectrum of highly enantioenriched alcohols.


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