



HOKKAIDO UNIVERSITY

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**Development of Phosphine-Branched Polystyrenes and
Their Applications to Transition-Metal Catalysis**

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General Introduction

1. Heterogeneous Transition-Metal Catalyst

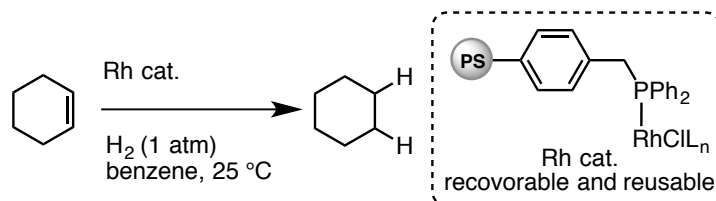
Transition-metal catalysts are powerful tools in organic synthesis. However, high cost and toxicity of transition metals are unfavorable for their applications into industrial or fine chemical organic synthesis. Immobilization of transition metal catalysts onto solid supports is one of the most effective ways to solve these problems. Facile separation of the catalysts by simple filtration is attractive for minimizing efforts to remove the metal residue from the product. Reuse of the immobilized catalyst is favorable for realizing sustainable synthetic process.

Various solid supports have been used for heterogeneous transition metal catalysts. They are mainly classified into three classes; organic polymers¹, inorganic materials and organic-inorganic hybrid materials. Organic polymers have benefits over the other solid supports in their structural diversity, physical property and chemical stability. Among a large number of organic polymers, polystyrene (PS) is the most common polymer support for transition metal catalysts owing to its easy preparation, ready availability and facile functionalization.

2. Polystyrene-Supported Phosphine Ligands

Attaching a tertiary phosphine, which is one of the most popular ligands for transition metals, to organic polymers such as polystyrene is a common strategy for preparation of heterogenized catalysts. In 1971, Grubbs and co-worker firstly reported a catalytic use of a PS-supported phosphine-metal complex² (Scheme 1). An immobilized Rh complex bearing PS-PPh₃ catalyzed hydrogenation of alkenes with a comparable activity to the homogeneous RhCl(PPh₃)₃ complex. The catalytic system could be reused at least 10 times without loss of the activity. Since this seminal report, a large number of PS-supported phosphines were used for catalytic reactions. However, in many cases, their catalytic activities were only comparable, or decrease, to those of homogeneous counterparts, due to unfavorable steric effects of polymer chains to the active site. Thus, using the PS backbone for an increase in catalytic activity is practically attractive, but still difficult.

Scheme 1. Polystyrene-supported phosphine and its catalytic use

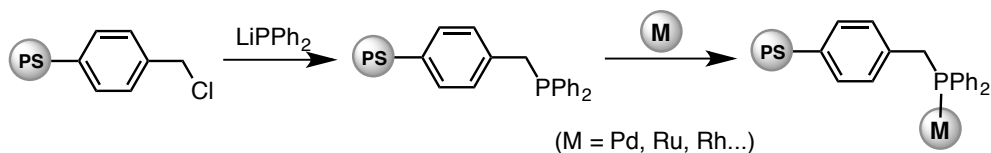


2.1 Preparation method

2.1.1 Grafting on functionalized polystyrene

Polystyrene-supported phosphines have the advantage of facile preparation. The simplest way is grafting of a phosphine moiety on chloromethyl-functionalized polystyrene, such as Merrifield resin (Scheme 2).

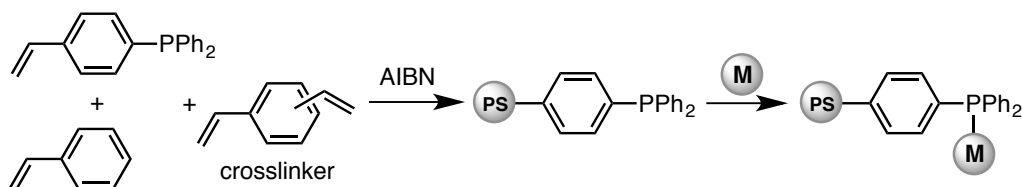
Scheme 2. Preparation through a grafting method



2.1.1 Copolymerization with cross-linker

The other method to prepare PS-supported phosphines is radical copolymerization with vinylated phosphine, styrene monomer and cross-linker (e.g. divinylbenzene). In this procedure, the ratio of components can be modified. Accordingly, physical properties of polymer supports are tunable.

Scheme 3. Preparation through radical copolymerization with styrene monomer



In 1999, Seebach and co-worker developed an excellent method for reducing steric hindrance of polymer chains toward catalytic sites bound to PS, albeit not using phosphine ligands. The PS-supported TADDOL-based ligands with a dendritic spacer for chiral Lewis acid catalysts were prepared through copolymerization of styrene

monomers with multi-vinylated TADDOL derivatives^{3a} (Figure 1). Owing to the multi-fold cross-linking, the catalytic sites have large space for easy access of substrates. In fact, activities and stereoselectivities of these immobilized catalysts were comparable to their homogeneous counterparts. After that, Seebach and coworkers applied this strategy to BINOL^{3b}- and SALEN^{3c}- based ligands.

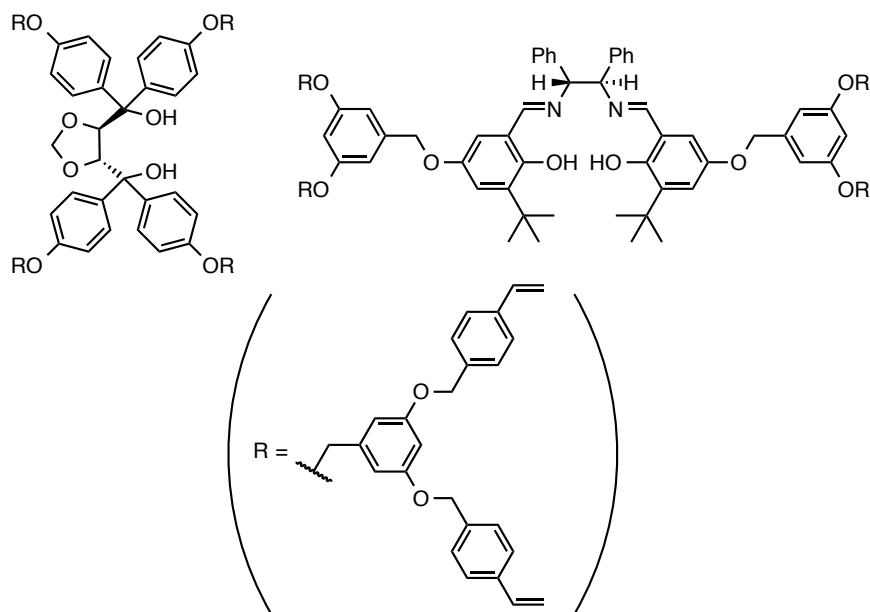
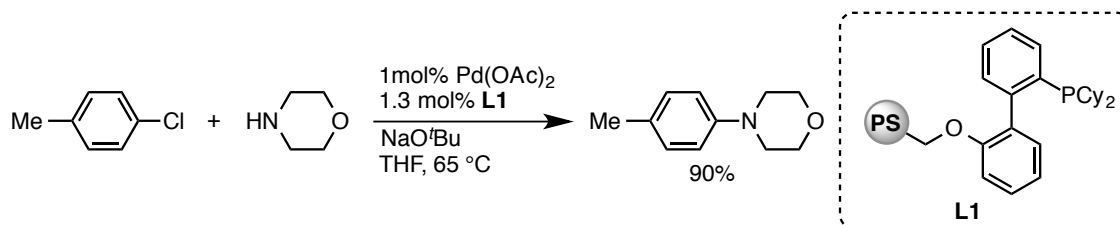


Figure 1. Dendritic TADDOL and Saren ligands as cross-linkers.

2.2 Immobilization of alkylphosphines

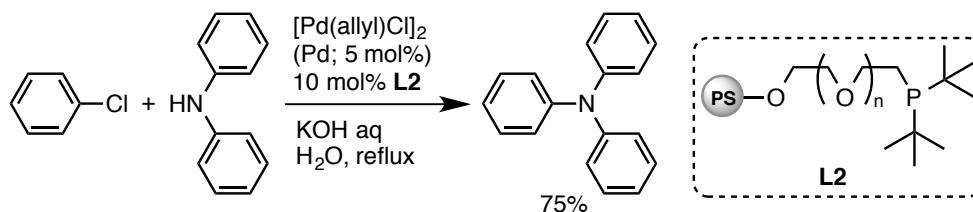
Alkylphosphines have a strong electron-donation property than arylphosphines. Such feature is useful for various transition-metal catalysis including Pd-catalyzed cross-coupling reactions. In 2001, Buchwald and co-worker have synthesized a PS-supported (dialkylphosphino)biphenyl ligand (Scheme 4)⁴. The Pd catalyst with this ligand enabled Buchwald-Hartwig amination reactions of aryl chlorides, for which use of conventional PS-supported triarylphosphines is difficult⁵.

Scheme 4. PS-supported dialkylphosphinobiphenyl and its use to Pd-catalyzed C-Cl cross-coupling reaction.



Uozumi and co-worker developed a di(*t*-butyl)-substituted phosphine ligand grafted on the PS-PEG chain^{6b} (Scheme 5). This ligand was significantly effective for Pd-catalyzed Buchwald-Hartwig amination of aryl chlorides under aqueous conditions, giving triaryl amines in high yield without metal contamination.

Scheme 5. Pd-catalyzed triarylamine synthesis in water with an amphiphilic PS-PEG-supported alkylphosphine.



Although these phosphines realized challenging catalytic transformations on the polymer-support, these catalytic performances are comparable to those of homogeneous counterparts. In these cases, there were no improvements on catalytic activity over homogenous ones.

2.3 Functionalization of polystyrene support

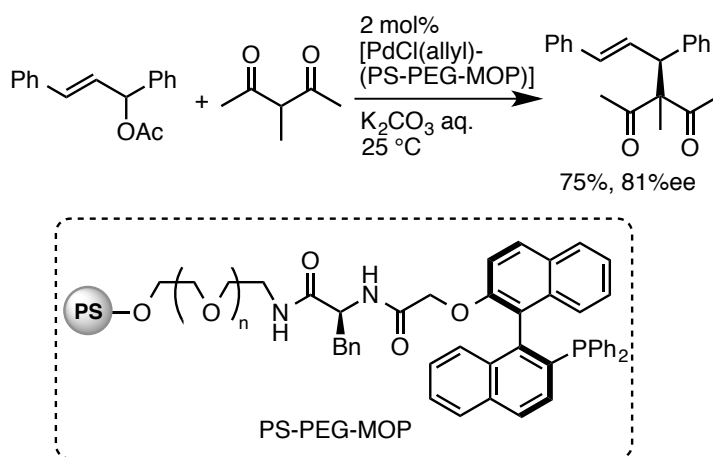
Functionalization of polystyrene supports can give additional features to catalytic system. Among them, several examples with advantages for environmentally benign organic synthesis are described below.

Introduction of hydrophilic substituents or backbone on the polymer enhances their swelling property toward polar solvents such as water. These features enable the

catalytic reaction in water solvent. Water is recognized as environmentally benign and cheaper solvent compared to toxic and expensive organic solvents.

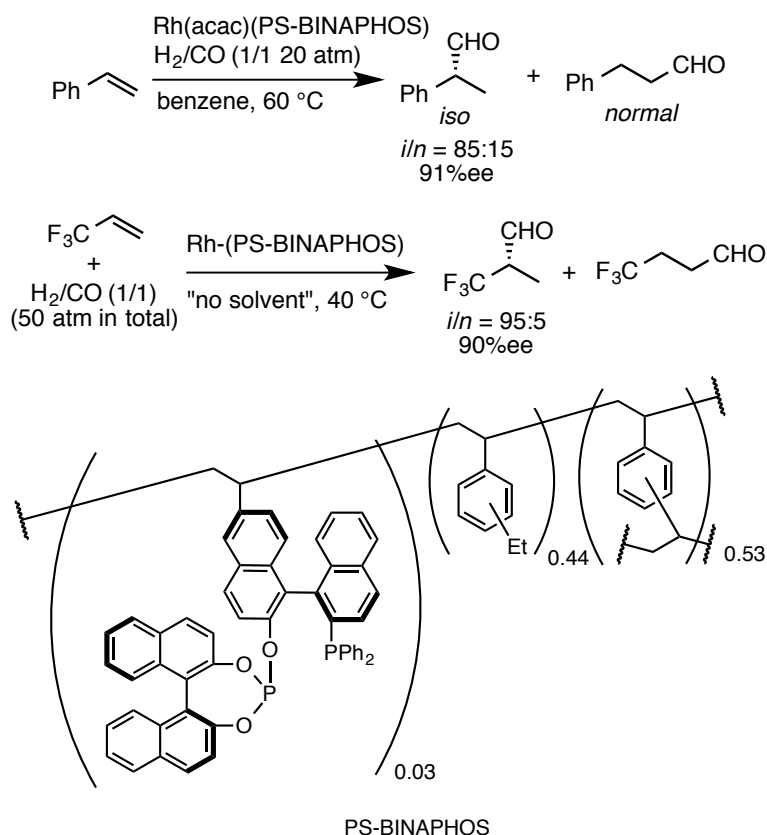
In 1999, Hayashi and Uozumi has developed a polystyrene-poly(ethylene glycol) (PS-PEG) immobilized phosphine for catalytic reaction in aqueous phase^{6b}. They attached a MOP ligand (Monodentate Optically active Phosphine, MOP) onto the amphiphilic resin. The Pd complexes with this polymeric ligand realized excellent reactivity and enantioselectivity in asymmetric allylic substitution in water (Scheme 6).

Scheme 6. Pd-catalyzed allylic substitution in water



Solvent-free reactions are also green synthetic processes. In 1998, Nozaki and co-worker reported that immobilized Rh complexes with PS-BINAPHOS, which was a heterogeneous chiral phosphine-phosphite ligand, efficiently catalyzed asymmetric hydrofomylation of olefins under CO/H₂ atmosphere with excellent reactivity and enantioselectivity^{7f} (Scheme 7). The successful gas-phase reaction was attributed to the nature of large pore volume and surface area of the highly cross-linked polystyrene resin.

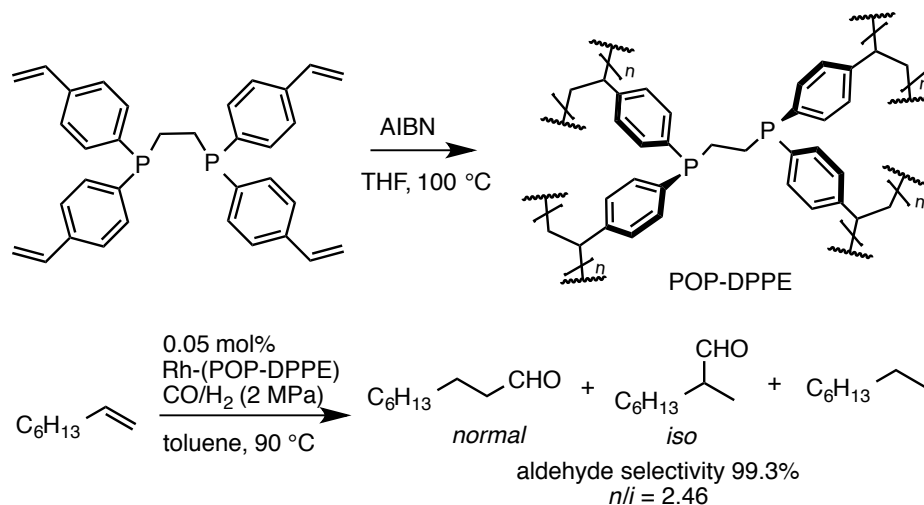
Scheme 7. Rh-(PS-BINAPHOS)-catalyzed asymmetric hydroformylation of olefins



2.4 Porous organic polymer.

Recently, porous organic polymers have received much attention as a new well-defined polymeric support for transition metal catalyst owing to their high surface areas and pore volumes⁸. In 2015, Xiao and co-worker synthesized a series of phosphines immobilized on porous organic polymers (POP) through solvothermal polymerization of multivinylated phosphines (Scheme 8). The obtained polymers showed good swelling properties to various solvents. Owing to these characteristics, these phosphine polymers exhibited higher reactivity and selectivity than homogeneous counterparts in Rh-catalyzed hydroformylation of olefins^{8b}.

Scheme 8. POP-ligand for Rh-catalyzed hydroformylation of olefins.

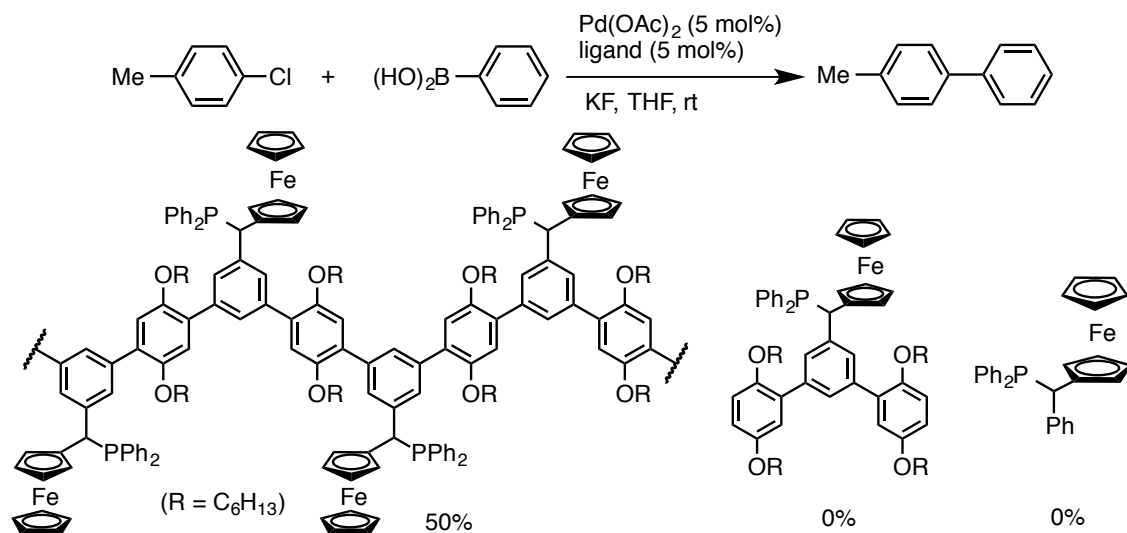


3. Design of polymer-supported phosphines for site isolation of catalytic center

Organic polymers have an advantage in flexible tuning and facile functionalization of the polymer backbone over other solid supports such as silica gel or zeolite. Taking these advantages, several sophisticated-polymer supported phosphines were designed and synthesized for effective site isolation to date. Such spatially isolated phosphine ligands would be favorable not only to generate coordinatively unsaturated catalytically active species but also to prevent intermolecular deactivation pathways, resulting in generation of highly active heterogeneous transition metal catalyst systems even with considerable synthetic efforts. This section describes recent advance on this field. The similar examples using inorganic solids as a support are also summarized.

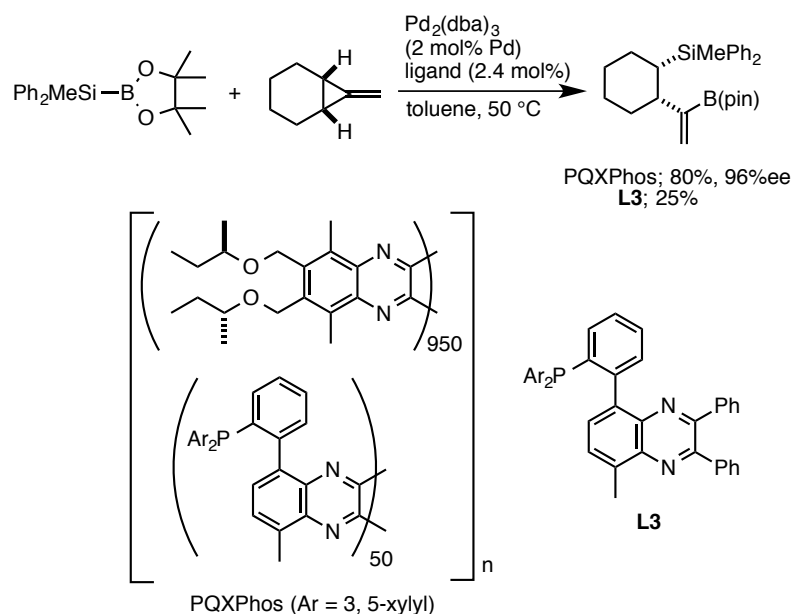
In 2003, Hu and co-workers reported that a ferrocenylmethyl phosphine-containing polymer⁹ was an effective ligand for the Pd-catalyzed Suzuki–Miyaura cross-coupling reactions of unactivated chloroarenes at room temperature^{9a} (Scheme 9). The rigidity of the polymer allowed effective site isolation of each phosphine center to form active mono-P-ligated Pd(0) species. In contrast, the monomeric phosphines with the same unit did not promote the coupling reaction at all.

Scheme 9. Pd-catalyzed Suzuki–Miyaura cross-coupling of chloroarene with a ferrocenylmethyl phosphine-containing macromolecule.



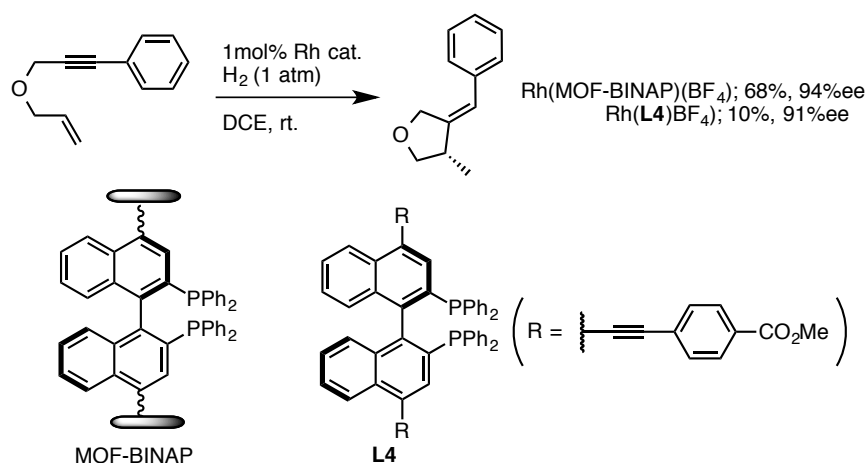
In 2011, Suginome and coworkers reported that the poly(quinoxaline)-based helically chiral phosphine ligand PQXphos¹⁰ enabled the Pd-catalyzed asymmetric silaboration of methylenecyclopropanes with high enantioselectivity and activity^{10c} (Scheme 10). In contrast, its phosphine monomer analogue showed much less reactivity for this transformation. These results indicated that the helical polymer might serve not only as a chiral center but also as a platform to generate active Pd species.

Scheme 10. Helical polymer-immobilized phosphine PQXphos for Pd-catalyzed silaboration of methylenecyclopropanes.



Recently, metal organic frameworks (MOF), which are structurally well-defined and rigid polymers, have become suitable platforms for efficient heterogeneous catalysts¹¹. Lin and co-worker designed and synthesized BINAP-based MOFs as new heterogeneous chiral ligands¹². The MOF-based Rh complexes showed not only excellent enantioselectivity but also higher catalytic activity than homogeneous counterparts in asymmetric reductive cyclization of 1,6-ene-yne (Scheme 11).

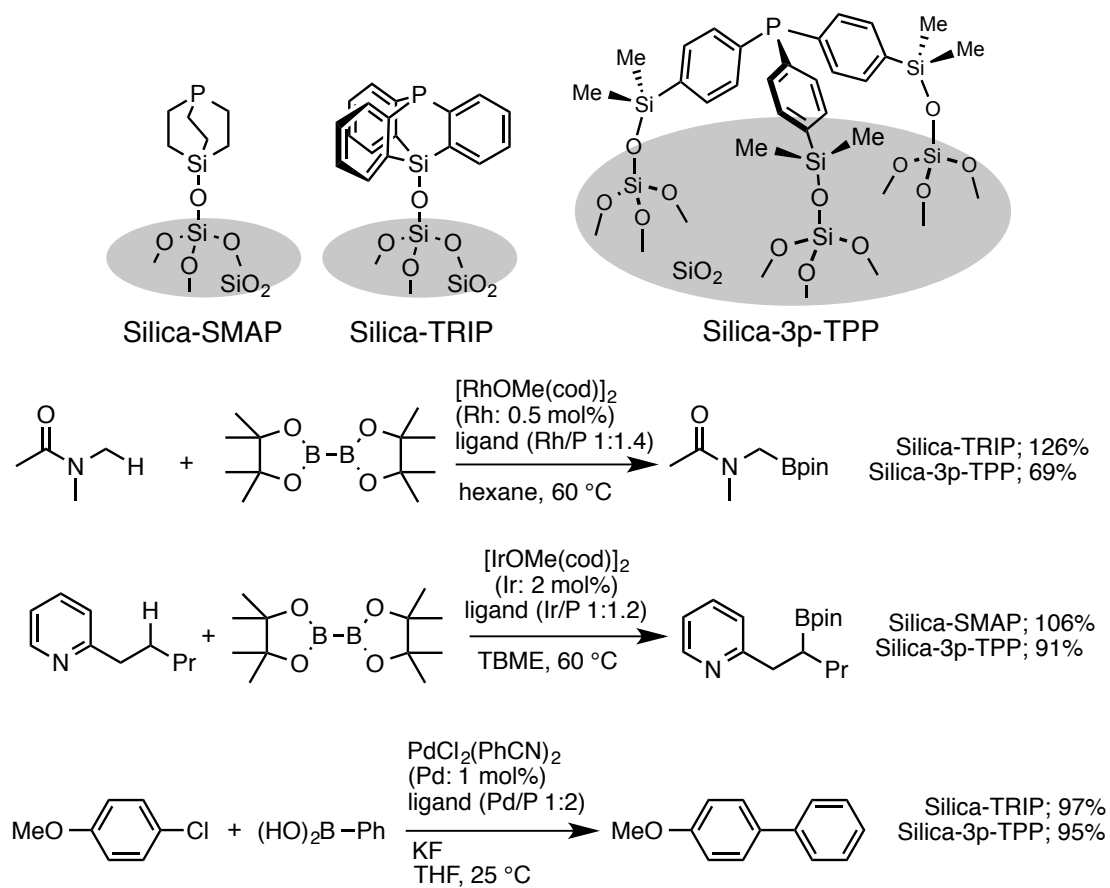
Scheme 11. MOF-BINAP ligand for Rh-catalyzed reductive cyclization of 1,6-ene-yne



Sawamura and coworkers developed a series of phosphine ligands attached onto a silica gel surface directly. The silica-supported caged phosphines such as Silica-SMAP¹³ and Silica-TRIP¹⁴ have the least mobility on the silica gel surface (Scheme 12). These ligands enabled site isolation of each ligand molecules, and thus these ligands could form mono-P-ligated metal complexes selectively. Accordingly, these ligands exhibited excellent performance toward challenging transformations such as Rh or Ir-catalyzed C(sp²)-H and C(sp³)-H borylation reactions¹⁵ as well as Pd-catalyzed C-Cl cross-coupling reactions¹⁶. In all cases, immobilization of the ligands were crucial, all homogeneous counterparts were totally ineffective.

More recently, Sawamura's group developed the second-generation immobilized phosphine Silica-3p-TPP, which features a triphenylphosphine core tripodally immobilized on silica gel directly. Silica-3p-TPP showed comparable performance to silica-supported caged phosphines in various transformations^{15i,16bc}. The multipod immobilization of the simple triarylphosphine ligand was also effective for site isolation.

Scheme 12. Silica gel-immobilized monophosphines developed by Sawamura



4. Overview of This Thesis.

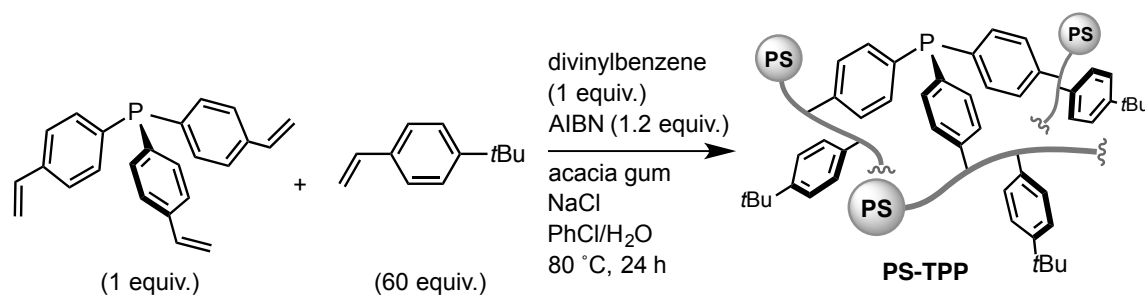
4.1 Introduction

In this thesis, the author describes the development of phosphine-branched polystyrene as a novel approach to generate catalytically active monoligated phosphine-metal complexes. Specifically, multi-vinylated phosphines (monophosphine and bisphosphine) are copolymerized with styrene monomers, giving polystyrene having the coordination centers at cross-linking points. The structural feature enables efficient site isolation of transition-metal complexes. Such metal complexes were found to exhibit excellent catalytic activities toward challenging transformations involving unreactive $C(sp^2)-Cl$, $C(sp^2)-O$ and $C(sp^3)-H$ bond activation. This protocol realizes production of highly active species with a simple ligand design and minimal synthetic efforts. Therefore, the author believes that the studies in this thesis would become a new guideline of ligand design for efficient and practical transition-metal catalysis.

4.2 Threefold Cross-Linked Polystyrene-Triphenylphosphane Hybrids: Mono-P-Ligating Behavior and Catalytic Applications for Aryl Chloride Cross-Coupling and $C(sp^3)-H$ Borylation (Chapter 1).

Chapter 1 describes the development of PPh_3 -branched polystyrene PS-TPP, as a new type of polystyrene-supported phosphine ligands. PS-TPP was synthesized through radical emulsion copolymerization¹⁷ with styrene monomer, divinylbenzene and trivinylated PPh_3 (Scheme 13). The coordination property toward a $Pd(II)$ complex suggested that PS-TPP could form a phosphine/metal 1:1 complex selectively.

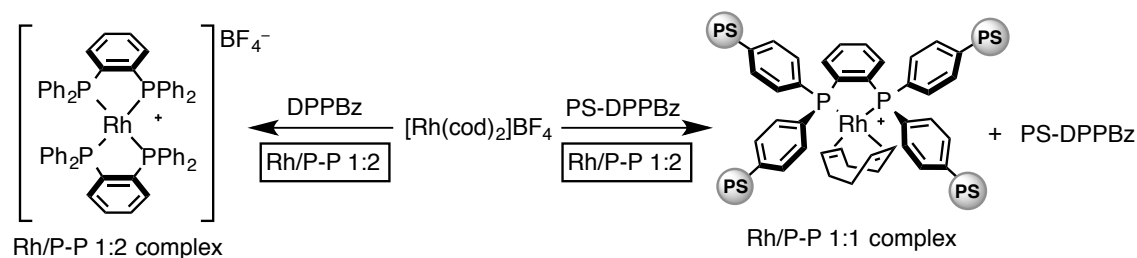
Scheme 13. Preparation of PS-TPP



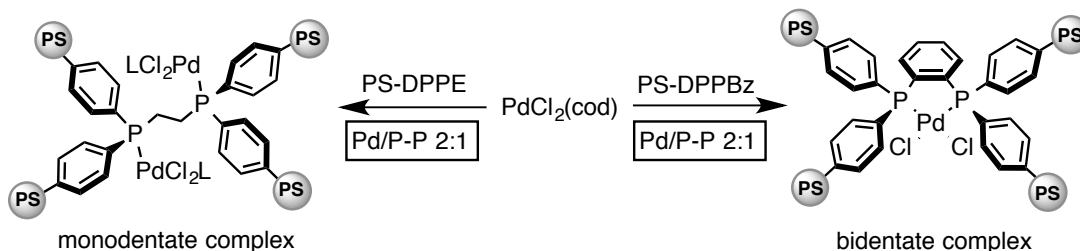
PS-TPP exhibited excellent ligand performance toward the Pd -catalyzed $C(sp^2)-Cl$ cross-coupling as well as Rh - or Ir -catalyzed $C(sp^3)-H$ borylation (Scheme 14) despite

The reactions of PS-DPPBz with a cationic Rh(I) complex or a Pd(II) complex demonstrated its mono-chelation property (Scheme 16). The importance of the rigid *o*-phenylene scaffold for the chelate coordination was confirmed by a control experiment with PS-DPPE, which has a flexible ethylene linker to connect two P atoms (Scheme 17).

Scheme 16. Coordination properties of PS-DPPBz and DPPBz toward a cationic Rh(I) complex.



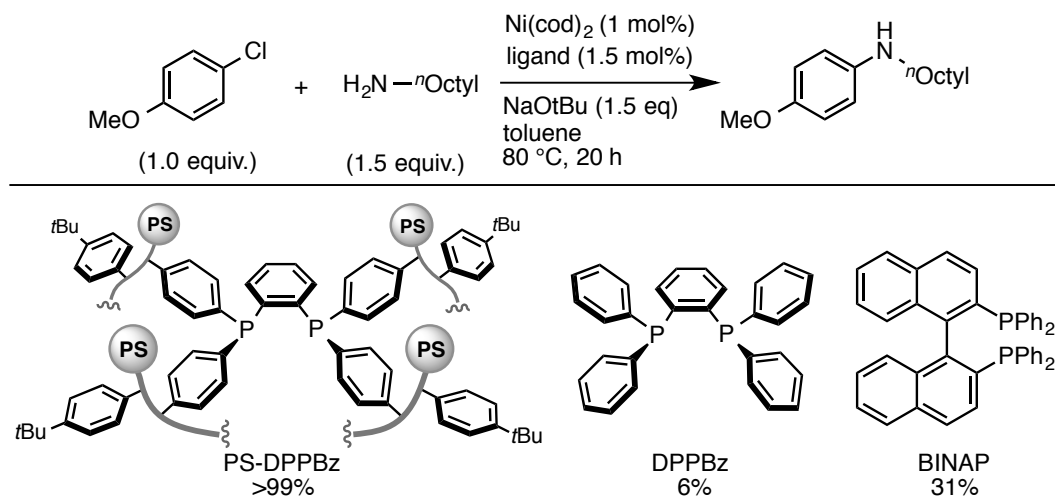
Scheme 17. Coordination property of PS-DPPBz and PS-DPPE toward a Pd(II) complex.



4.4 Ni-PS-DPPBz-catalyzed Amination of Aryl Chlorides with Primary Alkyl Amines (Chapter 3)

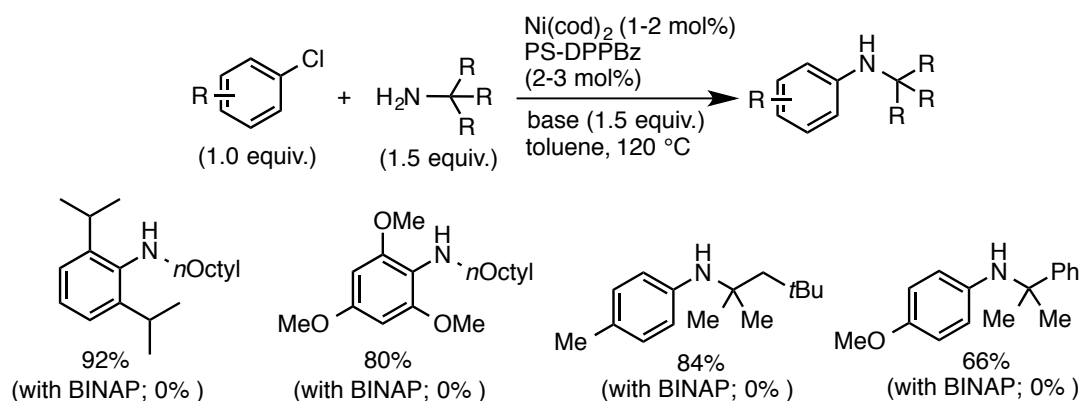
Chapter 3 describes that bisphosphine-branched polystyrene PS-DPPBz enabled the Ni-catalyzed amination of aryl chlorides with primary alkylamines^{20,21}. Owing to polymer effects to bisphosphine-bound active Ni centers, the Ni-PS-DPPBz system exhibited higher catalytic efficacy than homogeneous Ni-bisphosphine catalysts (Scheme 18).

Scheme 18. Ligand effect for Ni-catalyzed amination of aryl chlorides



Notably, the utility of the Ni-PS-DPPBz system was highlighted in the reactions with electron-donating and/or sterically congested substrates, for which reported protocols were not applicable (Scheme 19).

Scheme 19. Reactions of electron-donating and/or sterically congested substrates



4.5 Ni-PS-DPPBz-catalyzed Direct C–H Arylation of 1,3-Azoles with Aryl Pivalates (Chapter 4)

Chapter 4 describes that PS-DPPBz enabled the efficient Ni-catalyzed direct C–H arylation of 1,3-azoles with aryl pivalates. For this reaction, an electron-rich and bulky bisphosphine DCYPE is known as a specifically effective ligand²² to activate unreactive $\text{C}(\text{sp}^2)\text{--O}$ bond of aryl esters^{22,23}. Regardless of moderate electronic and steric natures based on the DPPBz-type ligand, PS-DPPBz exhibited comparable ligand

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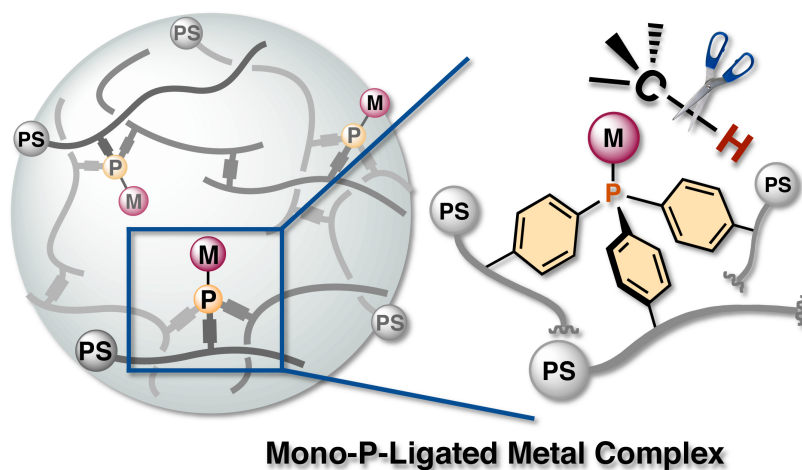
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Chapter 1.

Threefold Cross-Linked Polystyrene–Triphenylphosphine Hybrids: Mono-P-Ligating Behavior and Catalytic Applications for Aryl Chloride Cross-Coupling and C(sp³)–H Borylation



Abstract

Covalently bound polystyrene–phosphine hybrids were prepared by a method based on radical emulsion polymerization of styrenes in the presence of a tris(*p*-vinylphenyl)phosphine cross-linker. These hybrids favor mono-P-ligation to transition-metal complexes and are useful for challenging catalysis, such as Pd-catalyzed C–C/C–N couplings with unactivated chloroarenes and Ir- or Rh-catalyzed C(sp³)–H borylations.

Introduction

Polystyrene(PS)-supported phosphines are widely used for heterogeneous transition-metal catalysis, taking advantage of their practical merits as insoluble materials.^[1,2] Owing to the flexible nature of the PS backbone, the phosphine moieties have generally significant mobility even in cross-linked PS resins, and thus exhibit ligand properties generally similar to those of their homogeneous counterparts, except for their insoluble nature. Thus, such supported phosphines are able to function not only as monodentate ligands (Figure 1, A) but also as bidentate or multidentate ligands (Figure 1, B) toward transition metals. In many cases, however, the flexible polymer chain causes unfavorable steric effects in the catalytic environment, resulting in reduced catalyst efficiency (Figure 1, C). Thus, using the PS backbone for designing phosphine ligands to favor a specific structure desirable for an increase in catalytic activity is difficult.

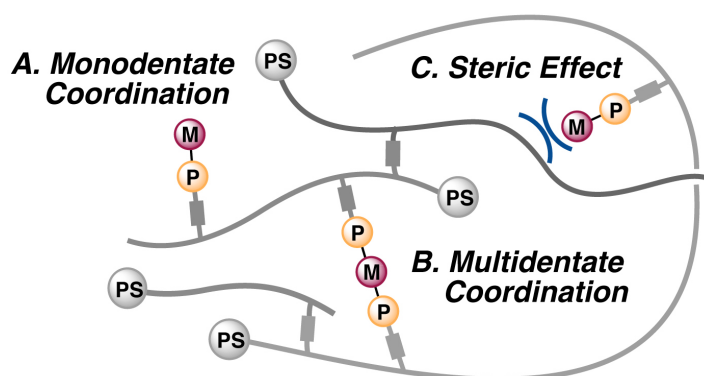


Figure 1. A conceptual view of various metal coordination modes of a PS-supported phosphine. The PS chains, which may cause steric effects toward the catalytic environment, are shown as gray lines.

This chapter describes a new type of polystyrene–phosphine covalently bound hybrid, which was prepared through radical emulsion polymerization of styrenes in the presence of tris(*p*-vinylphenyl)phosphine as a threefold cross-linker.^[3–5] The scenario is as follows: The threefold cross-linking increases the density of the polymer chain around the Ph_3P core, and thus limits multidentate P-coordination to the metal, but the steric demand in proximity to the P atom is only moderate (Ph_3P -like) owing to the

spacer effect of the three aromatic rings on the P atom, which projects toward trigonal pyramid directions; consequently, the resulting mono-P-ligated metal system allows effective access of substrates for catalysis. In fact, this simple technique yielded novel immobilized mono- dentate tertiary phosphine ligands that specifically formed mono-ligated transition-metal complexes (Figure 2). The successful Pd-catalyzed C–Cl transformation reactions such as Suzuki–Miyaura coupling and Buchwald–Hartwig amination as well as the Ir- or Rh-catalyzed C(sp³)–H borylation reaction demonstrated the utility of this strategy, suggesting that steric hindrance of the polymer chain unfavorable for catalytic performance was successfully reduced in this system.

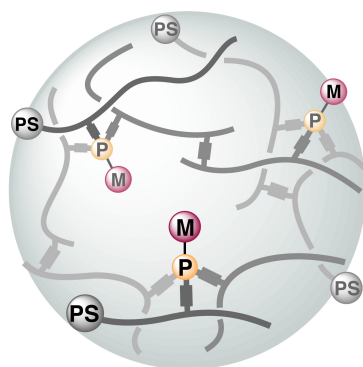


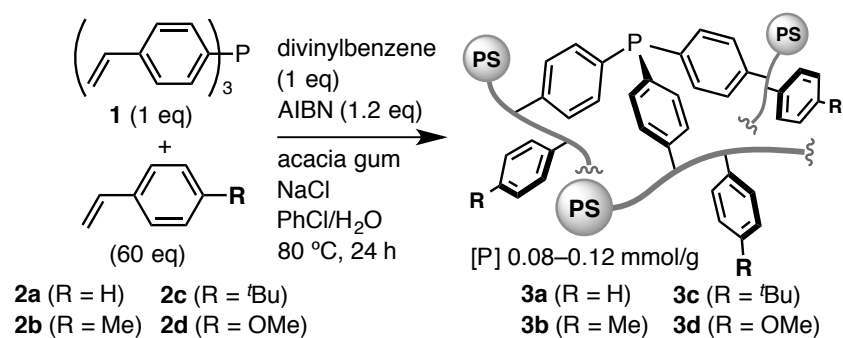
Figure 2. A conceptual view of metal mono-P-ligation of a networked PS resin prepared from a phosphine-centered threefold cross-linker. PS chains are shown as gray lines.

Results and Discussion

A solution of tris(*p*-vinylphenyl)phosphine (**1**), divinylbenzene (DVB), monofunctional styrenes (**2a–d** : R = H, Me, *t*Bu, OMe), and AIBN (azobis(isobutyronitrile); **1**/DVB/**2**/AIBN 1:1:60:1.2; stoichiometry not optimized) in chlorobenzene was dispersed in an aqueous phase containing acacia gum and NaCl.^[7] The mixture was vigorously stirred at 80 °C for 24 h for 70–90 % consumption of the vinyl monomers. The resultant solids were collected by filtration, washed with water, MeOH, THF, and toluene, and dried under vacuum to provide the Ph₃P cross-linked PS (**3a–d**) as white beads (Scheme 1). The polymer beads did not contain any solvent molecules or unreacted monomers that were detectable by ¹³C CP/MAS NMR spectroscopy (Figure 3). The phosphorus loading values ([P] 0.08–0.12 mmol g^{−1}) were

determined based on their abilities to capture transition-metal complexes.^[8] DVB (not shown in **3**) was used as a co-cross-linker to achieve uniform formation of bead-shape materials.

Scheme 1. Preparation of the Ph₃P-cross-linked PS (**3a–d**).



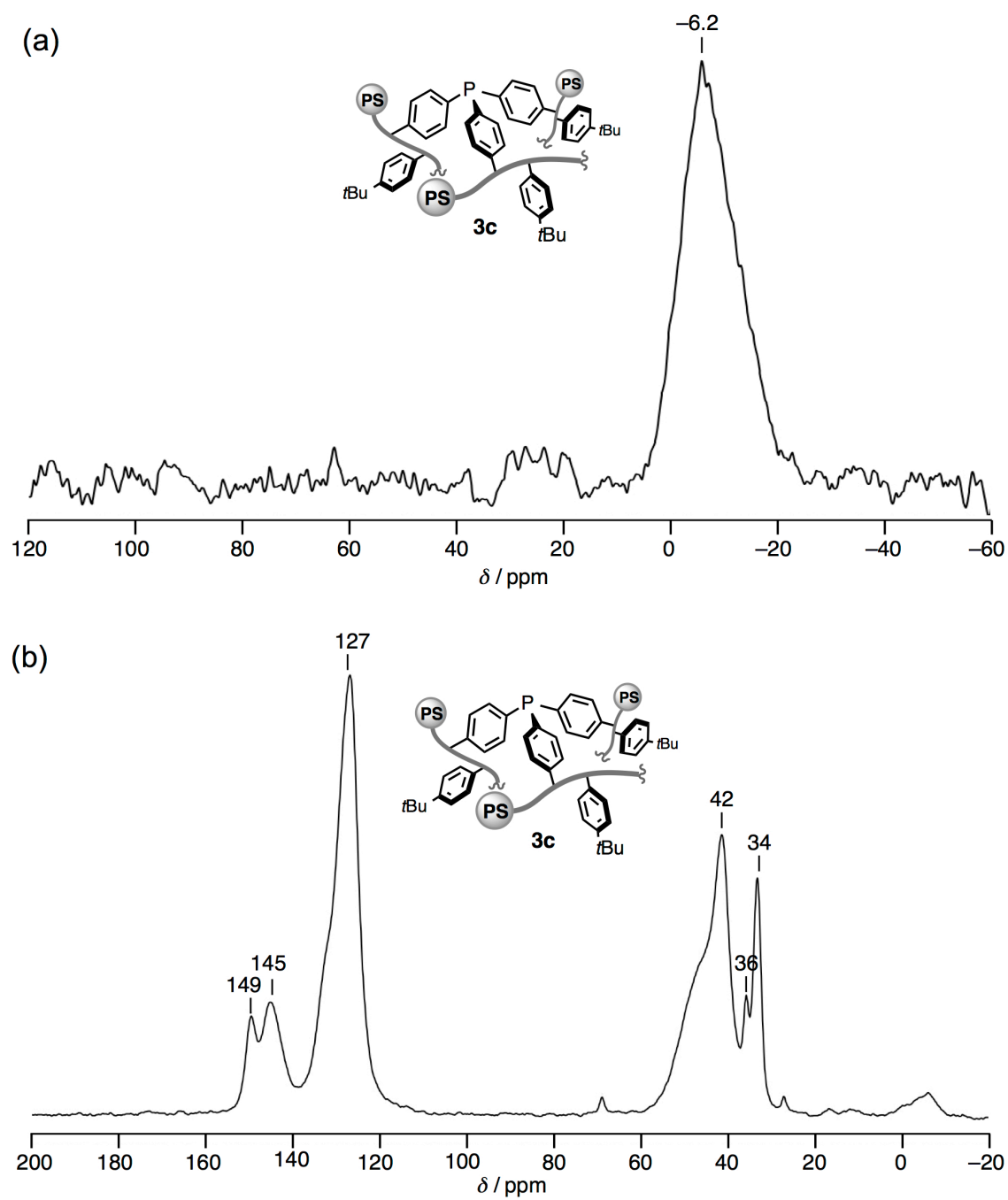


Figure 3. (a) ^{31}P CP/MAS and (b) ^{13}C CP/MAS spectra of **3c**.

The dried beads of **3** have diameters of about 300–400 μm (Figure 4a), and exhibited ordinary swelling properties as polystyrene resins. The swelling properties of the PS- Ph_3P hybrids **3a–d**, **4**, **5** in various solvents are summarized in Table 1. Swelling was good with aprotic solvents, such as toluene, THF, and CH_2Cl_2 (Figure 4b), but poor with aliphatic hydrocarbons and aprotic polar or protic solvents such as DMF, MeOH, and water. The degree of swelling was slightly dependent on the substituent (R) on the benzene ring of the PS backbone (5.0–5.8 mL g^{-1} in toluene).

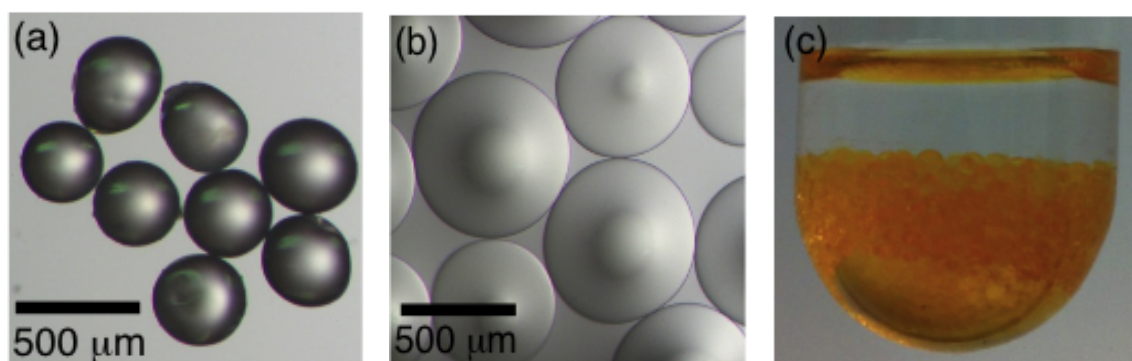


Figure 4. (a) Dried beads of **3c** (R = *t*Bu). (b) Beads of **3c** swollen in toluene. (c) Beads of $[\text{PdCl}_2(\text{PhCN})(\mathbf{3c})]$ with a stirring bar as prepared in THF (P/Pd 2:1).

Table 1. Swelling properties of the PS resins (**3–5**) in various solvents (volume in mL/g)

solvent	3a	3b	3c	3d	4	5
toluene	5.0	5.8	5.8	5.0	5.2	5.6
benzene	5.4	6.2	6.0	4.8	5.8	6.2
CPME	4.6	5.6	5.9	3.7	6.4	5.4
THF	6.0	4.4	5.0	4.6	5.2	5.2
CH_2Cl_2	4.5	4.0	4.0	4.2	4.0	4.1
hexane	1.8	2.2	2.4	1.8	2.6	2.6
DMF	3.2	2.0	2.1	4.0	2.0	2.2
MeOH	2.0	2.2	2.0	2.3	2.2	2.2
H_2O	2.4	2.0	2.4	2.0	2.0	2.4

The treatment of the THF-swollen polymer beads **3c** with $[\text{PdCl}_2(\text{PhCN})_2]$ at room temperature under magnetic stirring caused gradual coloring of the beads to orange over several minutes (Figure 4c). The ^{31}P CP/MAS NMR analysis (Figure 5) was clearly indicative of the selective formation of the mono-P-ligated Pd^{II} complex $[\text{PdCl}_2(\text{PhCN})(\mathbf{3c})]$, irrespective of the stoichiometry of the P ligand and the Pd source (P/Pd 2:1, 1:2). In contrast, the homogeneous reaction between $[\text{PdCl}_2(\text{PhCN})_2]$ and 2 equiv of (*p*-Tol) $_3\text{P}$ in THF gave bis-P-ligated complex $\text{trans-}[\text{PdCl}_2\{(\textit{p}\text{-Tol})_3\text{P}\}_2]$ as a single product. Similarly, the conventional PS-supported phosphine **5** (chemical structure shown in Scheme 2), in which the phosphine moiety was incorporated in the PS resin through the reaction of monovinylated triphenylphosphine, gave the bis-P-ligated complex $[\text{PdCl}_2(\mathbf{5})_2]$ as a major species when P was in excess (P/Pd 2:1) (Figure 6.).

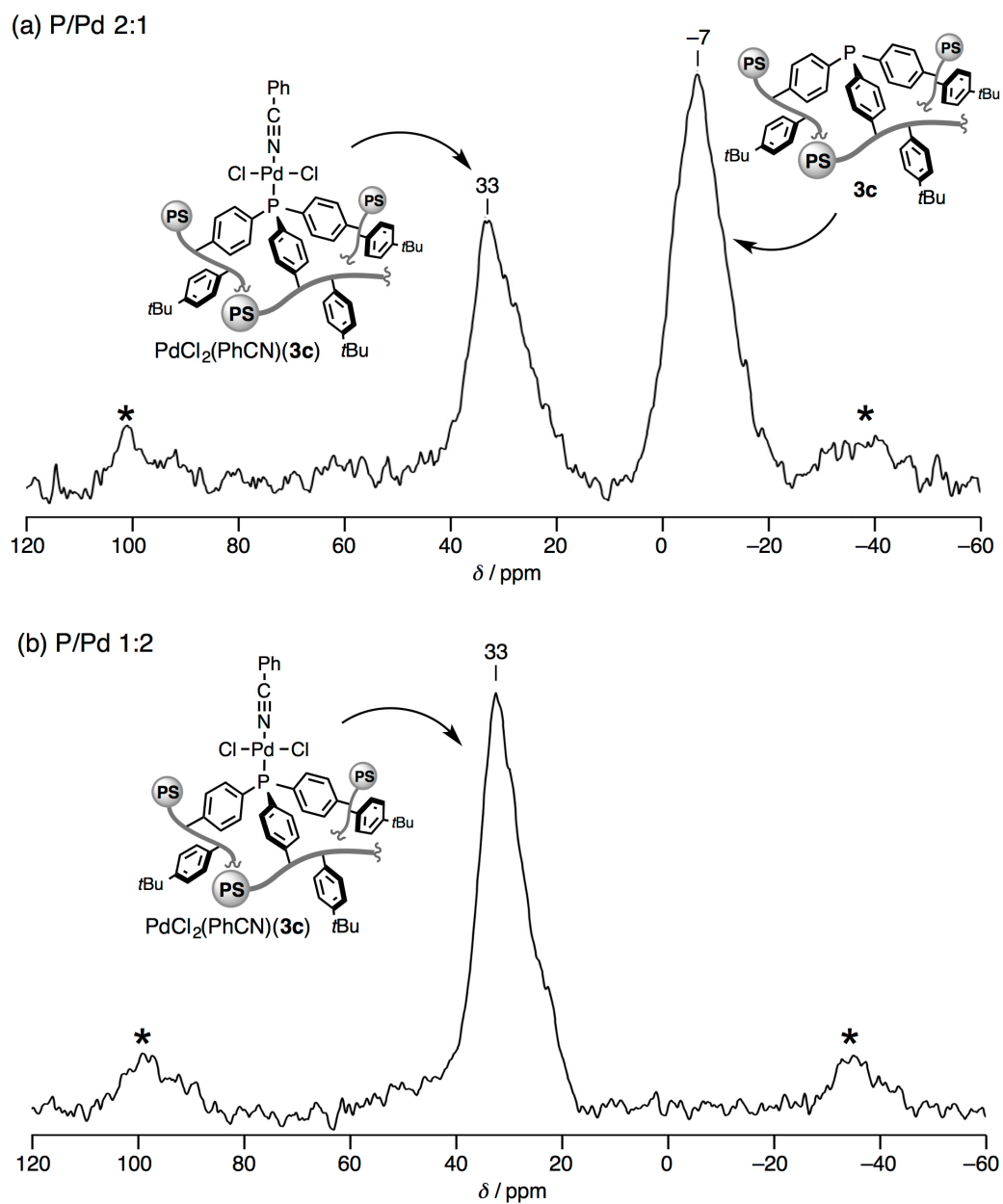


Figure 5. ^{31}P CP/MAS NMR spectra obtained after the reaction of **3c** and $[\text{PdCl}_2(\text{PhCN})_2]$ (P/Pd (a) 2:1 and (b) 1:2). Asterisks(*) indicate spinning side bands.

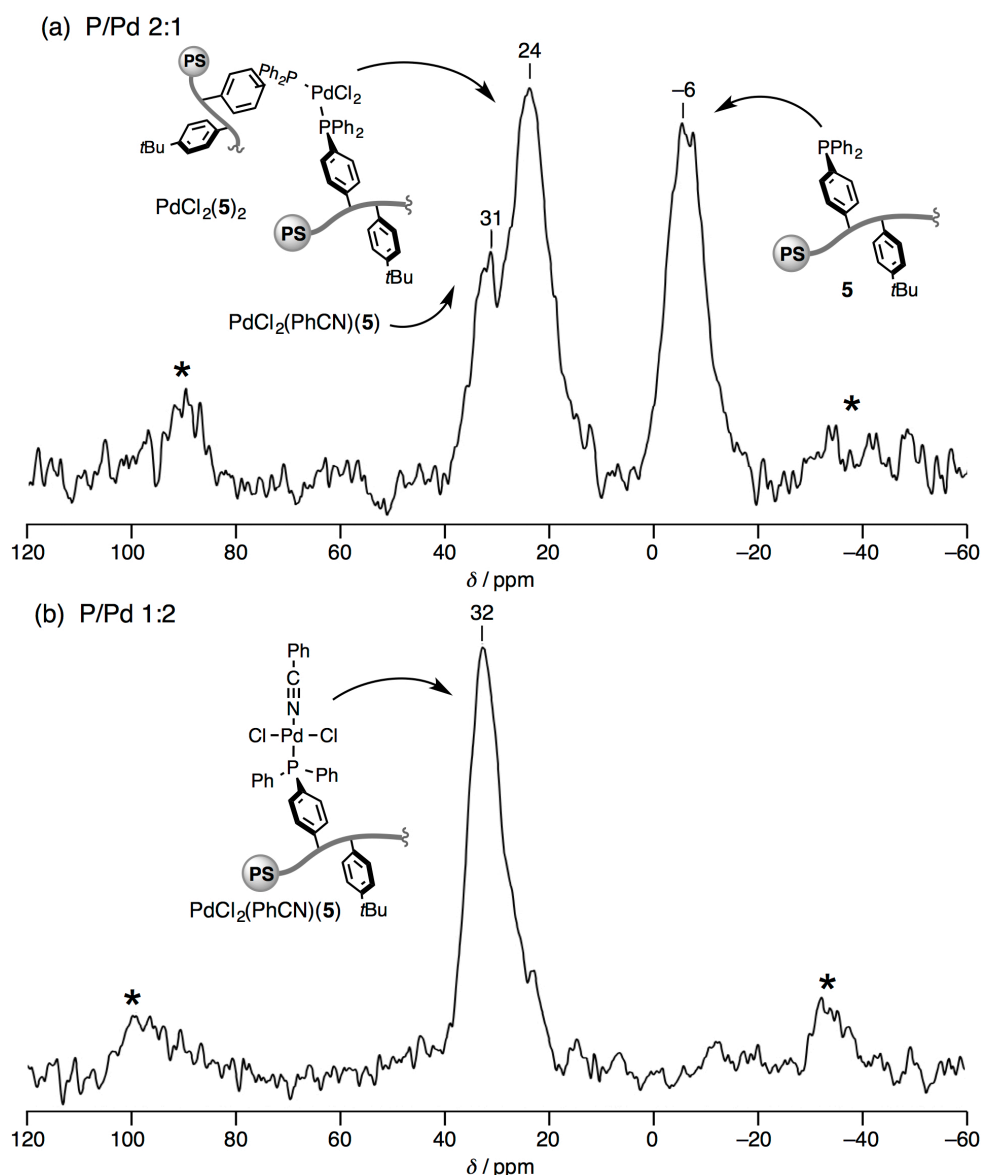
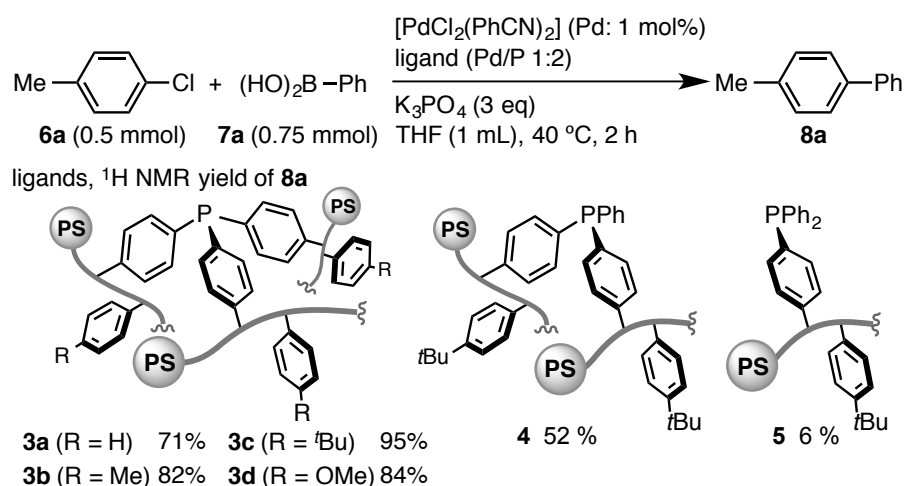


Figure 6. ^{31}P CP/MAS NMR spectrum obtained after the reaction of **5** and $[\text{PdCl}_2(\text{PhCN})_2]$ (P/Pd (a) 2:1 and (b) 1:2). Asterisks(*) indicate spinning side bands.

Controlled mono-ligation in the Pd-3 systems having been confirmed, we explored their applicability toward Suzuki–Miyaura coupling of unactivated chloroarenes, for which the importance of mono-ligation of two-electron donor ligands has been well-established through experiments with bulky and electron-rich phosphine^[9, 10] or NHC^[11] ligands. Furthermore, Tsuji and co-workers achieved mono-ligation of Ph_3P -based ligands by introducing steric demands in the periphery of the dendrimer-type high-molecular-weight phosphine molecules.^[12–14] In fact, these “bowl-shaped” phosphines also induced the Suzuki–Miyaura coupling with chloroarenes.^[12b]

The mono-P-ligated Pd^{II} complexes [PdCl₂(PhCN)(**3a–d**)] (1 mol% Pd) were evaluated for catalytic efficacy in the coupling reaction between *p*-chlorotoluene (**6a**, 0.5 mmol) and phenylboronic acid (**7a**, 0.75 mmol) in the presence of K₃PO₄ (1.5 mmol). To his delight, the reaction proceeded under mild conditions (THF, 40 °C, 2 h, Scheme 2). The yield of biaryl **8a** was apparently dependent on the substituents (R) on the benzene ring of the PS backbone of **3**. Relatively high yields were obtained with the substituted ligands (**3b**, R = Me, 82%; **3c**, R = *t*Bu, 95%; **3d**, R = OMe, 84%) compared with the parent ligand (**3a**, R = H, 71%). The origin of these substituent effects are not clear; it is not explained by the difference in the swelling properties.

Scheme 2. Effect of PS-supported triarylphosphines in the Pd-catalyzed Suzuki–Miyaura cross-coupling reaction.



The threefold cross-linking is essential. The analogous twofold cross-linked PS-Ph₃P hybrid **4** (R = *t*Bu) gave **8a** in only 52 % yield under otherwise identical conditions, and the conventional single-point linked PS-Ph₃P hybrid **5** was even less efficient (6 % yield ; Scheme 2). A homogeneous catalyst system based on Ph₃P did not induce the reaction at all (data not shown).

The heterogeneous catalyst system prepared from [{PdCl(η^3 -cinnamyl)}₂] (1 mol % Pd) and **3c** (2 mol% P) was examined for reusability in the coupling reaction between **6a** (1.0 mmol) and **7a** (1.5 mmol ; K₃PO₄, 60 °C, 2 h).^[15] After the first run, the catalyst beads were contaminated with inorganic salts, and the supernatant was colorless.

The insoluble materials were filtered, washed with H₂O, and then with THF, and dried under vacuum to obtain orange- colored catalyst beads for use in the next run. The Pd-**3c** catalyst maintained most of its activity even in the fourth run, but the gradual color change from orange to brown over repeated uses (yield of **8a**: 1st 91%, 2nd 97%, 3rd 98%, 4th 94 %, 5th 85 %).^[16, 17] HRTEM observation of the reused Pd-**3c** was indicative of gradual formation of Pd cluster species, which should be less active or inactive (Figure 7).^[18] Inductively coupled plasma atomic emission spectroscopy (ICPAES) analysis indicated that Pd leaching for each run was below the detection limit (< 0.02 % of the loaded Pd).^[19]

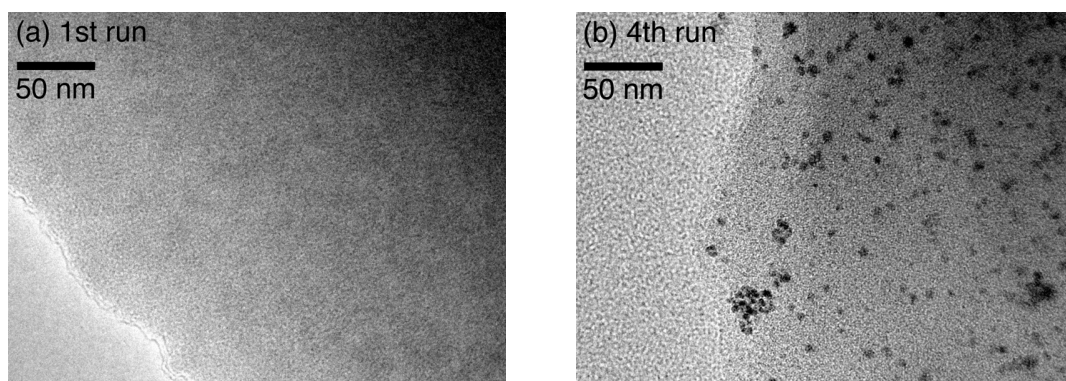


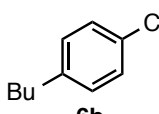
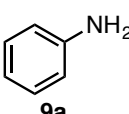
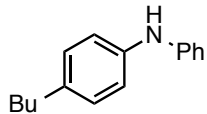
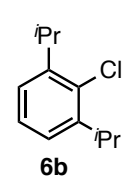
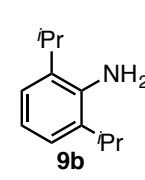
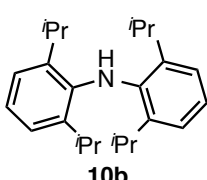
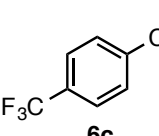
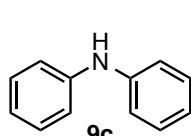
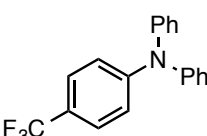
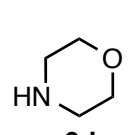
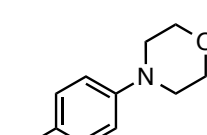
Figure 7. (a,b) HR-TEM images of part of the Pd-**3c** resins after 1st and 4th runs, respectively.

The chemical stability of the PS resin and the C-C bond linkage between the phosphine moiety and the resin is the advantage of the PS-Ph₃P hybrids **3** over heterogenized ligands based on oxide surfaces in the cases of using them under rather harsh reaction conditions. For example, a catalyst system prepared from [$\text{PdCl}(\eta^3\text{-allyl})\}_2$] (1.5 mol % Pd) and **3c** (3 mol % P) was successfully applied to the amination of *p*-butylchlorobenzene (**6b**, 0.25 mmol) with aniline (**9a**, 0.3 mmol).^[20] The reaction was conducted under basic and high-temperature conditions employing KO^tBu (0.35 mmol), which is stronger base than K₃PO₄, and a toluene-^tBuOH (4:1) mixture as the base and solvent, respectively, at 100 °C over 20 h to afford the corresponding diarylamine **10a** in 80 % yield (Table 2).^[21] Notably, when the previously reported silica-supported monophosphines (silica-SMAP^[22] and silica-TRIP^[23]) with similar

mono-P-ligating features were applied to this Pd catalysis instead of the PS-Ph₃P hybrid, the complete leaching of metal and P atoms owing to degradation of the oxide surface was evident, and no substrate conversion was observed, showing the merit of the PS resin over silica gel as a robust solid support. It is also to be noted that use of the twofold cross-linked phosphine **4**, the single-point linked phosphine **5**, and the homogeneous ligand **1** were again less efficient (22%, 5%, and 0% yields, respectively).^[24]

This procedure was also applicable for the synthesis of a sterically congested diarylamine (**10b**) and a triarylamine (**10c**, from diphenylamine). The amination of the chloroarene **6b** with morpholine to give the N,N-dialkylaniline derivative **10d** was successfully performed under even more basic conditions using LiHMDS as a base.

Table 2. The C–N coupling reactions with the Pd-**3c** catalyst system.

$ \begin{array}{c} \text{Ar-Cl} \quad + \quad \text{HNR}^1\text{R}^2 \\ \textbf{6} \quad \quad \quad \textbf{9} \\ (0.25 \text{ mmol}) \quad (0.3 \text{ mmol}) \end{array} \xrightarrow[\text{base (1.4 eq) condition}]{\begin{array}{c} [\{\text{PdCl(allyl)}\}_2] \text{ (Pd: 1.5 mol\%)} \\ \textbf{3c} \text{ (P: 3 mol\%)} \end{array}} \text{Ar-NR}^1\text{R}^2 \\ \textbf{10} $					
entry	Ar-Cl 6	HNR ₁ R ₂ 9	condition	Product 10	yield (%)
1			KOtBu, toluene/tBuOH (4:1) 100 °C, 20 h		80
2			KOtBu, toluene/tBuOH (4:1) 100 °C, 20 h		80
3			KOtBu, toluene/tBuOH (4:1) 110 °C, 20 h		75
4	6b		LHMDS, toluene 60 °C, 20 h		67

The mono-ligating feature of the threefold cross-linked PS-Ph₃P hybrids (**3**) and their excellent performance in the Pd-catalyzed coupling reactions prompted us to test the best-performing ligand **3c** in the heteroatom-directed borylation of unactivated C(sp³)-H bonds, for which the silica-supported cage-type trialkyl- or triarylphosphines (silica-SMAP and silica-TRIP, respectively) were effective ligands in recent studies of the author's group.^[22c,e,f, 23] The author expected that such experiments might give an answer to the question as to whether or not the cage in silica-SMAP and silica-TRIP is essential.

In fact, the PS-Ph₃P hybrid **3c** did promote these challenging catalyses. Specifically, the reaction of 2-pentyl- pyridine (**11**) with bis(pinacolato)diboron (**12**) in the presence of a catalytic amount of [$\{\text{Ir}(\text{OMe})(\text{cod})\}_2$] (2 mol % Ir) and **3c** (2 mol % P) afforded secondary alkylboronate **13** in 82 % yield based on the diboron **12** (Table 3, entry 1).^[24f] Although the twofold cross-linked PS-Ph₃P ligand **4** and the single-point linked ligand **5** also induced the borylation, their efficacies were significantly lower than that of the threefold cross-linked ligand **3c** (entries 2 and 3). No reaction occurred under homogeneous conditions with Ph₃P (entry 4).

Table 3. Ir-catalyzed C(sp³)-H borylation.

$$\text{11 (3 eq)} + \text{B}_2\text{pin}_2 \xrightarrow[\text{CPME, 60 } ^\circ\text{C, 15 h}]{[\{\text{Ir}(\text{OMe})(\text{cod})\}_2] \text{ (Ir: 2 mol\%)} \text{ Ligand (Ir/P 1:1)}} \text{13} + \text{pinB-H}$$

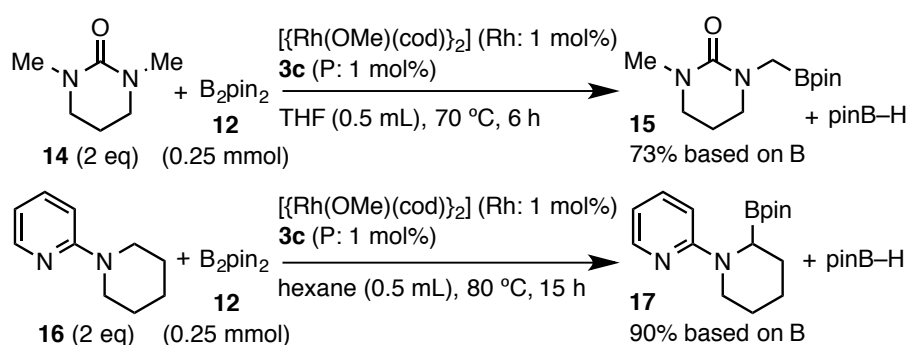
entry	ligand	Yield (%) ^b
1	3c	82
2	4	61
3	5	45
4	PPh ₃	0

^aConditions: **11** (0.9 mmol), **12** (0.3 mmol), [$\{\text{Ir}(\text{OMe})(\text{cod})\}_2$] (0.006 mmol Ir), ligand (0.006 mmol P), cyclopentyl methyl ether (CPME, 1 mL), 60 °C, 15 h. ^b Yield determined by ¹H NMR analysis based on **12**.

The threefold cross-linked PS-Ph₃P ligand **3c** was also effective for the Rh-catalyzed N-adjacent C(sp³)-H borylation of urea **14** and 2-aminopyridine **16** (1 mol % Rh, Scheme 3), for which the silica-TRIP triarylphosphine ligand was effective but the silica-SMAP trialkylphosphine was not in previous study of the author's group.^[23] As the pinB-H also served as a reagent for the C-H borylation, the a-aminoalkylboronates **15** and **17** were obtained in good or high yields (**15**, 73 %; **17**, 90%) based on the boron atom used. These results clearly show that achieving mono-P-ligation and having moderate ligand steric effect together is important for

producing a C(sp³)–H borylation catalyst (mono-P-ligating, homogeneous bulky phosphines were not useful^[22c,e,f,23]), and using a cage structure as in silica-SMAP and silica-TRIP is not always necessary. Advantages of the PS-Ph₃P hybrid system over the cage-type silica-supported phosphines are found in the easiness of the synthesis and structural modification and in the flexibility for expanding the concept.

Scheme 3. Rh-catalyzed N-adjacent C(sp³)–H borylation.



Conclusion

A new type of polystyrene(PS)–phosphine covalently bound hybrid was synthesized through radical emulsion copolymerization of styrenes, divinylbenzene, and a tris(*p*-vinylphenyl)phosphine threefold cross-linker. These hybrids were used for catalyst systems to favor a mono-P-ligated metal complex with minimal synthetic effort. The applicability of the PS-Ph₃P hybrids toward Pd-catalyzed cross-coupling reactions of unactivated chloroarenes as well as Ir- or Rh-catalyzed borylation reactions of C(sp³)–H bonds demonstrates the utility of this simple heterogeneous strategy.

Experimental Section

Instrumentation and Chemicals

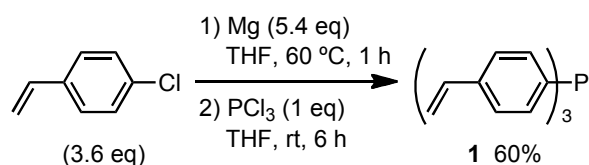
Solution NMR spectra were recorded on a Varian Gemini 2000 spectrometer, operating at 300 MHz for ¹H NMR, 75.4 MHz for ¹³C NMR and 121.4 MHz for ³¹P NMR. Chemical shift values for ¹H, ¹³C, and ³¹P NMR spectra are referenced to Me₄Si, the residual solvent, and 85% phosphoric acid, respectively. Magic angle spinning (MAS) NMR spectra were recorded on a Bruker MSL-300 spectrometer, operating at 75.4 MHz for ¹³C NMR and 121.4 MHz for ³¹P NMR. High-resolution mass spectra were recorded on a Thermo Fisher Scientific Exactive, JEOL JMS-T100LP mass

spectrometer or JEOL JMS-T100 GC mass spectrometer at the Instrumental Analysis Division, Equipment Management Center, Creative Research Institution, Hokkaido University. ICP-AES analyses were performed on a Shimadzu ICPE-9000. The samples for TEM analysis were prepared by placing a drop of THF colloidal solution of the materials onto a holey carbon-coated copper grid and allowing THF to be evaporated under air. TEM analysis was performed on a JEOL JEM-2100F with accelerating voltage of 200 kV. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F₂₅₄. Silica gel (Kanto Chemical Co., Silica gel 60 N, spherical, neutral) was used for column chromatography. GLC analyses were conducted on a Shimadzu GC-14B equipped with a flame ionization detector. Melting points were determined on a micro melting point apparatus (Yanaco: MP-500D) using micro cover glass.

All reactions were carried out under nitrogen or argon atmosphere. Materials were obtained from commercial suppliers or prepared according to standard procedures unless otherwise noted. Divinylbenzene (*m*- and *p*- mixture, contains ethylvinylbenzene and ethylbenzene, >50% GC (purity) and styrene monomers (**2a–d**) were purchased from TCI, and purified by passing through a basic alumina column. 2,2'-Azo bis(isobutyronitrile) (AIBN) was purified by recrystallization from Et₂O. Acacia [Gum Arabic] was purchased from Nacalai. [$\{\text{RhCl}(\text{cod})\}_2$], [$\{\text{Rh}(\text{OMe})(\text{cod})\}_2$], [$\{\text{Ir}(\text{OMe})(\text{cod})\}_2$], [$\text{PdCl}_2(\text{PhCN})_2$], [$\{\text{PdCl}(\eta^3\text{-allyl})\}_2$] and [$\{\text{PdCl}(\eta^3\text{-cinnamyl})\}_2$] were prepared according to the literature.^[25] All solvents for catalytic reactions were degassed via four freeze–pump–thaw cycles before use. PCl_3 was purified by distillation under argon atmosphere before use. Bis(pinacolato)diboron (**12**) was purchased from AllyChem Co., Ltd., and recrystallized from pentane before use.

Preparation of Homogeneous Ligands

Tris(*p*-vinylphenyl)phosphine (**1**)

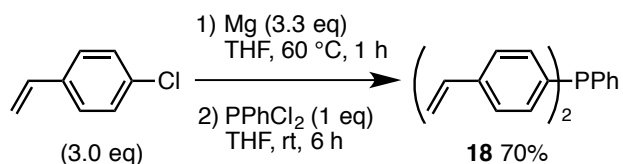


Although the title compound **1** was reported in the literature,^[3] the detailed preparation and spectral data were not described: Under argon, Mg turnings (1.31 g, 54

mmol, 5.4 eq) were placed in a 100-mL round-bottom flask equipped with a magnetic stirring bar, and were activated by treatment with 1,2-dibromoethane (10 μ L) in THF (24 mL). *p*-Chlorostyrene (4.99 g, 36 mmol, 3.6 eq) was added to the flask, and the mixture was stirred for 1 h at 60 °C. Next, PCl_3 (1.37 g, 10 mmol, 1 eq) was added to the solution over 5 min followed by stirring at room temperature for 6 h. After quenching with aq. NH_4Cl , the mixture was extracted with Et_2O . The organic layer was washed with water, dried over MgSO_4 , filtered and concentrated. The residue was purified by silica gel chromatography (4:1 hexane/ CH_2Cl_2) to give **1a** as white solids (2.04 g, 60% yield).

M.p.: 68.7–71.3 °C. ^1H NMR (CDCl_3): δ 5.28 (d, J = 10.7 Hz, 3H), 5.78 (d, J = 17.7 Hz, 3H), 6.71 (dd, J = 17.7, 10.7 Hz, 3H), 7.22–7.42 (m, 12H). ^{13}C NMR (CDCl_3): δ 114.77 (3C), 126.39 (d, $J_{\text{C-P}}$ = 7.2 Hz, 6C), 133.96 (d, $J_{\text{C-P}}$ = 19.2 Hz, 6C), 136.42 (3C), 136.69 (d, $J_{\text{C-P}}$ = 10.8 Hz, 3C), 138.06 (3C). ^{31}P NMR (CDCl_3): δ –6.3. **HRMS–ESI** (m/z): $[\text{M}+\text{H}]^+$ calcd for 341.14536; found, 341.14523.

Bis(*p*-vinylphenyl)phenylphosphine (**18**)^[5]

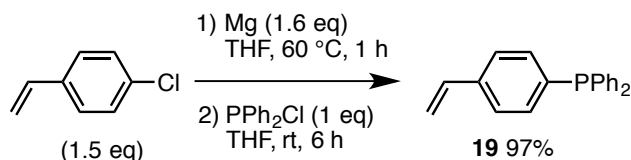


Under argon, Mg turnings (160 mg, 6.6 mmol, 3.3 eq) were placed in a 50-mL round-bottom flask equipped with a magnetic stirring bar, and were activated by treatment with 1,2-dibromoethane (10 μ L) in THF (3 mL). *p*-Chlorostyrene (832 mg, 6.0 mmol, 3.0 eq) was added to the flask, and the mixture was stirred at 60 °C for 1 h. Next, PPhCl_2 (358 mg, 2 mmol, 1 eq) was added to the solution over 5 min followed by stirring at room temperature for 6 h. After quenching with aq. NH_4Cl , the mixture was extracted with Et_2O . The organic layer was washed with water, dried over MgSO_4 , filtered and concentrated. The residue was purified by silica gel chromatography (4:1 hexane/ CH_2Cl_2) to give **18** as white solids (440 mg, 70% yield).

M.p.: 46.4–48.5 °C. ^1H NMR (CDCl_3): δ 5.28 (d, J = 11.2 Hz, 2H), 5.78 (d, J = 17.7 Hz, 2H), 6.71 (dd, J = 17.7, 11.2 Hz, 2H), 7.22–7.42 (m, 13H). ^{13}C NMR (CDCl_3): δ 114.69 (2C), 126.31 (d, $J_{\text{C-P}}$ = 6.9 Hz, 4C), 128.55 (d, $J_{\text{C-P}}$ = 6.9 Hz, 2C), 128.78, 133.70 (d, $J_{\text{C-P}}$ = 19.4 Hz, 2C) 133.93 (d, $J_{\text{C-P}}$ = 19.4 Hz, 4C), 136.36 (2C), 136.71 (d,

$J_{\text{C-P}} = 10.8 \text{ Hz}$, 2C), 137.12 (d, $J_{\text{C-P}} = 10.8 \text{ Hz}$), 137.94 (2C). ^{31}P NMR (CDCl_3): $\delta -5.7$.
HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for 315.12971; found, 315.12940.

Diphenyl(*p*-vinylphenyl)phosphine (19)^[26]

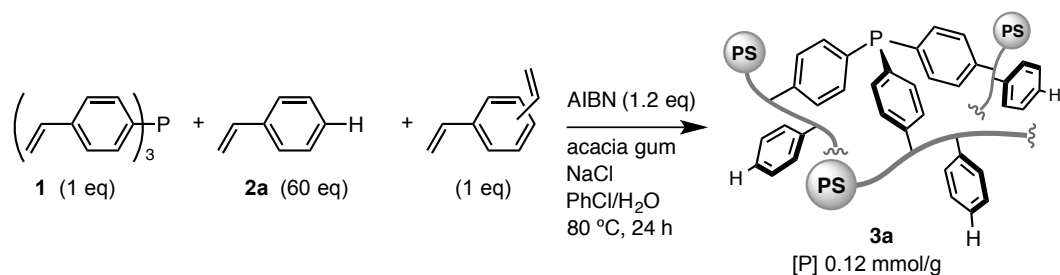


Under argon, Mg turnings (160 mg, 6.6 mmol, 1.6 eq) were placed in a 50-mL round-bottom flask equipped with a magnetic stirring bar, and were activated by treatment with 1,2-dibromoethane (10 μ L) in THF (3 mL). *p*-Chlorostyrene (832 mg, 6 mmol, 1.5 eq) was added to the flask, and the mixture was stirred at 60 $^{\circ}$ C for 1 h. Next, PPh₂Cl (882 mg, 4 mmol, 1 eq) was added to the solution over 5 min followed by stirring at room temperature for 6 h. After quenching with aq. NH₄Cl, the mixture was extracted with Et₂O. The organic layer was washed with water, dried over MgSO₄, filtered and concentrated. The residue was purified by silica gel chromatography (4:1 hexane/CH₂Cl₂) to give **19** as white solids (1.12 g, 97% yield).

¹H NMR (CDCl₃): δ 5.28 (d, *J* = 11.2 Hz, 1H), 5.78 (d, *J* = 17.7 Hz, 1H), 6.71 (dd, *J* = 17.7, 11.2 Hz, 1H), 7.22–7.42 (m, 14H). **¹³C NMR** (CDCl₃): δ 114.71, 126.34 (d, *J*_{C-P} = 6.9 Hz, 2C), 128.58 (d, *J*_{C-P} = 6.9 Hz, 4C), 128.81 (2C), 133.78 (d, *J*_{C-P} = 19.5 Hz, 4C), 134.01 (d, *J*_{C-P} = 19.5 Hz, 2C), 136.44, 136.64 (d, *J*_{C-P} = 10.5 Hz), 137.19 (d, *J*_{C-P} = 10.5 Hz, 2C), 137.99. **³¹P NMR** (CDCl₃): δ -5.3.

Preparation of PS-Supported Ligands

Preparation of 3a

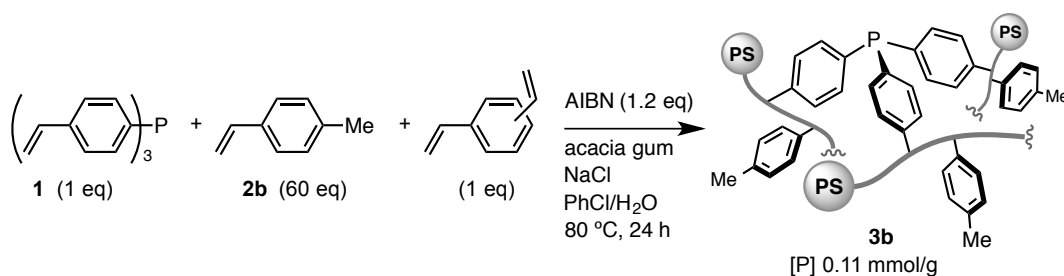


A solution of acacia gum (4.8 g) and NaCl (3.0 g) in water (120 mL) was placed in a 500-mL round-bottom flask equipped with a magnetic stirring bar, and was

deoxygenated by purging with Ar. On the other hand, a solution of styrene (**2a**, 3.1 g, 30 mmol), divinylbenzene (0.13 g, >50% purity, 0.5 mmol), **1** (0.17 g, 0.5 mmol) and AIBN (0.10 g, 0.6 mmol) in chlorobenzene (6 mL) was degassed by three freeze-pump-thaw cycles, and was injected into the rapidly stirred aqueous solution. The mixture was stirred at 80 °C for 24 h. After cooling to room temperature, the mixture was filtered through a glass adaptor equipped with a cotton plug, washed successively with H₂O, MeOH, THF and toluene, and dried in vacuo at 80 °C for 12 h to give the polymer **3a** as white beads (2.4 g, 71 wt%). A loading amount of phosphine ([P]) was determined to be 0.12 mmol/g based on the Rh to P stoichiometry of 1:1 (see, section 6).

³¹P CP/MAS: δ -6.9. ¹³C CP/MAS: δ 34–58 (–CHArCH₂–), 130 (*Ar*), 149 (*Ar*).

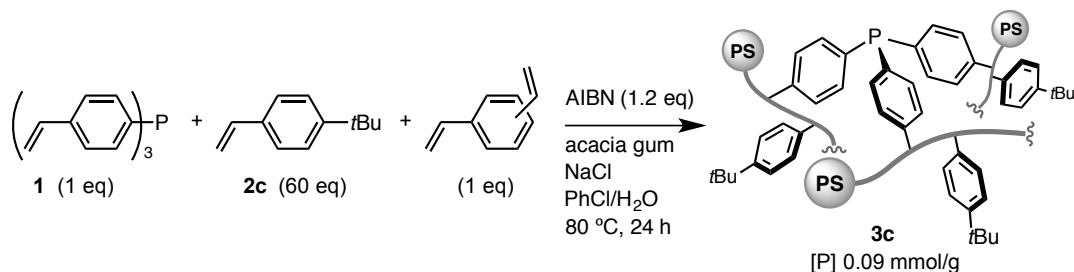
Preparation of 3b



A solution of acacia gum (4.8 g) and NaCl (3.0 g) in water (120 mL) was placed in a 500-mL round-bottom flask equipped with a magnetic stirring bar, and was deoxygenated by purging with Ar. On the other hand, a solution of *p*-methylstyrene (**2b**, 3.5 g, 30 mmol), divinylbenzene (0.13 g, >50% purity, 0.5 mmol), **1** (0.17 g, 0.5 mmol) and AIBN (0.10 g, 0.6 mmol) in chlorobenzene (6 mL) was degassed by three freeze-pump-thaw cycles, and was injected into the rapidly stirred aqueous solution. The mixture was stirred at 80 °C for 24 h. After cooling to room temperature, the mixture was filtered through a glass adaptor equipped with a cotton plug, washed successively with H₂O, MeOH, THF and toluene, and dried in vacuo at 80 °C for 12 h to give the polymer **3b** as white beads (2.9 g, 77 wt%). A loading amount of phosphine ([P]) was determined to be 0.11 mmol/g based on the Rh to P stoichiometry of 1:1 (see, section 6).

³¹P CP/MAS: δ -7.0. ¹³C CP/MAS: δ 23 (CH₃C₆H₄–), 34–57 (–CHArCH₂–), 131 (*Ar*), 136 (*Ar*), 145 (*Ar*).

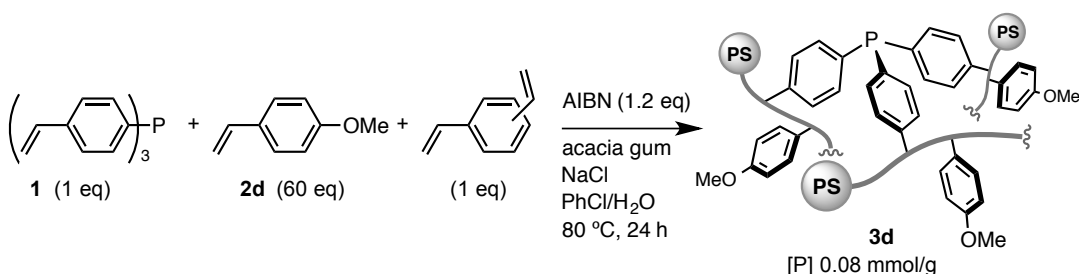
Preparation of 3c



A solution of acacia gum (4.8 g) and NaCl (3.0 g) in water (120 mL) was placed in a 500-mL round-bottom flask equipped with a magnetic stirring bar, and was deoxygenated by purging with Ar. On the other hand, a solution of *p*-(*tert*-butyl)styrene (**2c**, 4.8 g, 30 mmol), divinylbenzene (0.13 g, >50% purity, 0.5 mmol), **1** (0.17 g, 0.5 mmol) and AIBN (0.10 g, 0.6 mmol) in chlorobenzene (6 mL) was degassed by three freeze-pump-thaw cycles, and was injected into the rapidly stirred aqueous solution. The mixture was stirred at 80 °C for 24 h. After cooling to room temperature, the mixture was filtered through a glass adaptor equipped with a cotton plug, washed successively with H₂O, MeOH, THF and toluene, and dried in vacuo at 80 °C for 12 h to give the polymer **3c** as white beads (4.6 g, 90 wt%). A loading amount of phosphine ([P]) was determined to be 0.09 mmol/g based on the Rh to P stoichiometry of 1:1 (see, section 6).

³¹P CP/MAS: δ -6.2. ¹³C CP/MAS: δ 34 (-C(CH₃)₃), 36 (-C(CH₃)₃), 39–59 (-CHArCH₂-), 127 (*Ar*), 145 (*Ar*), 149 (*Ar*).

Preparation of 3d

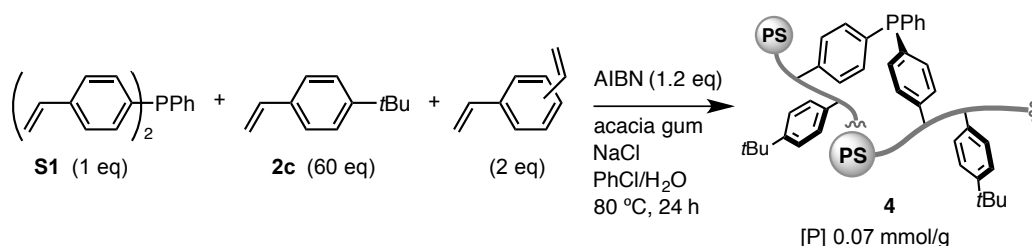


A solution of acacia gum (4.8 g) and NaCl (3.0 g) in water (120 mL) was placed in a 500-mL round-bottom flask equipped with a magnetic stirring bar, and was deoxygenated by purging with Ar. On the other hand, a solution of *p*-methoxystyrene

(**2d**, 4.0 g, 30 mmol), divinylbenzene (0.13 g, >50% purity, 0.5 mmol), **1** (0.17 g, 0.5 mmol) and AIBN (0.10 g, 0.6 mmol) in chlorobenzene (6 mL) was degassed by three freeze-pump-thaw cycles, and was injected into the rapidly stirred aqueous solution. The mixture was stirred at 80 °C for 24 h. After cooling to room temperature, the mixture was filtered through a glass adaptor equipped with a cotton plug, washed successively with H₂O, MeOH, THF and toluene, and dried in vacuo at 80 °C for 12 h to give the polymer **3d** as white beads (3.4 g, 78 wt%). A loading amount of phosphine ([P]) was determined to be 0.08 mmol/g based on the Rh to P stoichiometry of 1:1 (see, section 6).

³¹P CP/MAS: δ -6.5. ¹³C CP/MAS: δ 34–54 (–CHArCH₂–), 56 (CH₃OC₆H₄–), 115 (*Ar*), 129–143 (*Ar*), 160 (*Ar*).

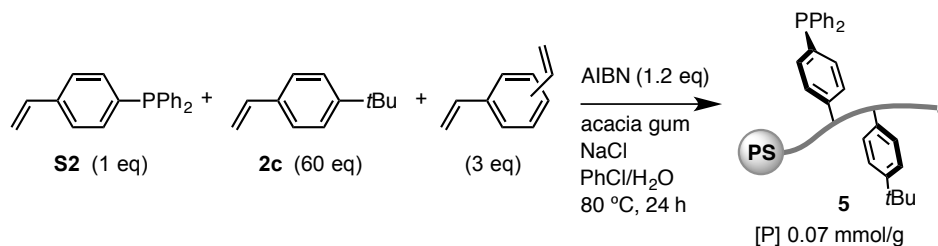
Preparation of 4



A solution of acacia gum (4.8 g) and NaCl (3.0 g) in water (120 mL) was placed in a 500-mL round-bottom flask equipped with a magnetic stirring bar, and was deoxygenated by purging with Ar. On the other hand, a solution of *p*-(*tert*-butyl)styrene (**2c**, 4.8 g, 30 mmol), divinylbenzene (0.26 g, >50% purity, 1 mmol), **S1** (0.16 g, 0.5 mmol) and AIBN (0.10 g, 0.6 mmol) in chlorobenzene (6 mL) was degassed by three freeze-pump-thaw cycles, and was injected into the rapidly stirred aqueous solution. The mixture was stirred at 80 °C for 24 h. After cooling to room temperature, the mixture was filtered through a glass adaptor equipped with a cotton plug, washed successively with H₂O, MeOH, THF and toluene, and dried in vacuo at 80 °C for 12 h to give the polymer **4** as white beads (4.5 g, 86 wt%). A loading amount of phosphine ([P]) was determined to be 0.07 mmol/g based on the Rh to P stoichiometry of 1:1 (see, section 6).

³¹P CP/MAS: δ -6.0. ¹³C CP/MAS: δ 33 (–C(CH₃)₃), 36 (–C(CH₃)₃), 38–58 (–CHArCH₂–), 127 (*Ar*), 145 (*Ar*), 150 (*Ar*).

Preparation of 5



A solution of acacia gum (4.8 g) and NaCl (3.0 g) in water (120 mL) was placed in a 500-mL round-bottom flask equipped with a magnetic stirring bar, and was deoxygenated by purging with Ar. On the other hand, a solution of *p*-(*tert*-butyl)styrene (**2c**, 4.8 g, 30 mmol), divinylbenzene (0.39 g, >50% purity, 1.5 mmol), **S2** (0.14 g, 0.5 mmol) and AIBN (0.10 g, 0.6 mmol) in chlorobenzene (6 mL) was degassed by three freeze-pump-thaw cycles, and was injected into the rapidly stirred aqueous solution. The mixture was stirred at 80 °C for 24 h. After cooling to room temperature, the mixture was filtered through a glass adaptor equipped with a cotton plug, washed successively with H₂O, MeOH, THF and toluene, and dried in vacuo at 80 °C for 12 h to give the polymer **5** as white beads (4.7 g, 87 wt%). A loading amount of phosphine ([P]) was determined to be 0.07 mmol/g based on the Rh to P stoichiometry of 1:1 (see, section 6).

³¹P CP/MAS: δ -5.7. ¹³C CP/MAS: δ 33 (-C(CH₃)₃), 36 (-C(CH₃)₃), 37–57 (-CHArCH₂-), 127 (*Ar*), 145 (*Ar*), 150 (*Ar*).

Large Scale Preparation of 3c.

A solution of acacia gum (24 g) and NaCl (15 g) in water (600 mL) was placed in a 2-L round-bottom flask equipped with a mechanical stirrer, and was deoxygenated by purging with Ar. On the other hand, a solution of *p*-(*tert*-butyl)styrene (**2c**, 24 g, 150 mmol), divinylbenzene (0.65 g, >50% purity, 2.5 mmol), **1** (0.85 g, 2.5 mmol) and AIBN (0.50 g, 3 mmol) in chlorobenzene (30 mL) was degassed by three freeze-pump-thaw cycles, and was injected into the rapidly stirred aqueous solution. The mixture was stirred at 80 °C for 24 h. After cooling to room temperature, the mixture was filtered through a glass adaptor equipped with a cotton plug, washed successively with H₂O, MeOH, THF and toluene, and dried in vacuo at 80 °C for 12 h to give the polymer **3c** as white beads (22 g, 86 wt%). A loading amount of phosphine ([P]) was determined to be 0.09 mmol/g based on the Rh to P stoichiometry of 1:1 (see,

section 6).

Swelling Tests of the PS Resins

Swelling tests of the PS resins were carried out according to the literature.^[29] A graduated 1-mL syringe equipped with a filter paper at the exit was charged with 100 mg of the PS resin (**3–5**, the original volume; ca. 1.8 mL/g), and an appropriate solvent (1 mL) was added to the resin. After the mixture was let stand for 15 min for equilibration, the extra solvent was removed from the syringe by using the plunger. The volume of the swollen resin was recorded

Determination of P Loadings

The PS resin **3c** (200 mg) and $[\{\text{RhCl}(\text{cod})\}_2]$ (9.7 mg, 0.02 mmol) were placed in a 5-mL vial tube. Anhydrous and degassed benzene (2 mL) was added to the tube, and the mixture was stirred at room temperature for 0.5 h. The suspension was filtered with a glass pipette equipped with a cotton plug, and washed successively with CH_2Cl_2 and Et_2O . The filtrate was evaporated and dried under vacuum to recover $[\{\text{RhCl}(\text{cod})\}_2]$ (5.3 mg). The yellow beads were dried under vacuum at 60 °C for 6 h to give $[\text{RhCl}(\text{cod})(\mathbf{3c})]$ (204 mg), which should contained 4.4 mg (9.7–5.3 mg) of $[\{\text{RhCl}(\text{cod})\}_2]$. Thus, the coordinatively active P loading on **3c** was determined to be 0.09 mmol/g based on the Rh to P stoichiometry of 1:1. The P loadings of the other PS-supported phosphines were determined with the identical procedure.

3a; [P] 0.12 mmol/g

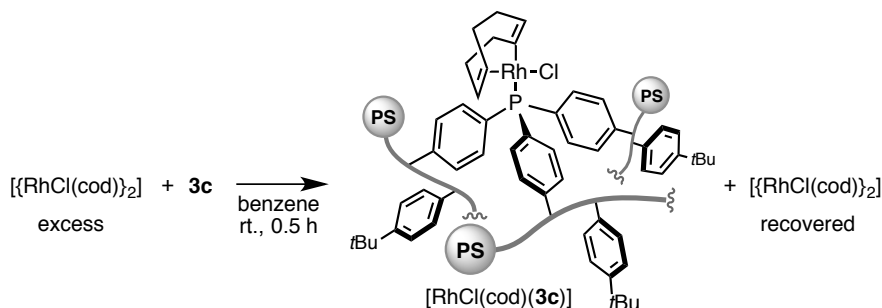
3b; [P] 0.11 mmol/g

3c; [P] 0.09 mmol/g

3d; [P] 0.08 mmol/g

4; [P] 0.07 mmol/g

5; [P] 0.07 mmol/g



NMR Studies for the Reactions of the PS-Supported Ligands and Pd(II) Complexes

The Reaction of PS resin **3a** and [PdCl₂(PhCN)₂] (P/Pd 2:1, 1:2).

The PS resin **3a** ([P] 0.12 mmol/g, 200 mg, 0.024 mmol) and [PdCl₂(PhCN)₂] (0.012 mmol for P/Pd 2:1, 0.048 mmol for P/Pd 1:2) were placed in a 5-mL vial tube. Anhydrous and degassed THF (2 mL) was added to the tube, and the mixture was stirred at room temperature for 0.5 h. The suspension was filtered with a glass pipette equipped with a cotton plug and washed successively with CH₂Cl₂ and Et₂O. The orange beads of the PS resin were dried under vacuum at 60 °C for 6 h, and analyzed by ³¹P CP/MAS NMR spectroscopy.

The Reaction of PS resin **3b** and [PdCl₂(PhCN)₂] (P/Pd 2:1, 1:2).

The PS resin **3b** ([P] 0.11 mmol/g, 200 mg, 0.022 mmol) and [PdCl₂(PhCN)₂] (0.011 mmol for P/Pd 2:1, 0.044 mmol for P/Pd 1:2) were placed in a 5-mL vial tube. Anhydrous and degassed THF (2 mL) was added to the tube, and the mixture was stirred at room temperature for 0.5 h. The suspension was filtered with a glass pipette equipped with a cotton plug and washed successively with CH₂Cl₂ and Et₂O. The orange beads of the PS resin were dried under vacuum at 60 °C for 6 h, and analyzed by ³¹P CP/MAS NMR spectroscopy.

The Reaction of PS resin **3c** and [PdCl₂(PhCN)₂] (P/Pd 2:1, 1:2)

The PS resin **3c** ([P] 0.09 mmol/g, 200 mg, 0.018 mmol) and [PdCl₂(PhCN)₂] (0.009 mmol for P/Pd 2:1, 0.035 mmol for P/Pd 1:2) were placed in a 5-mL vial tube. Anhydrous and degassed THF (2 mL) was added to the tube, and the mixture was stirred at room temperature for 0.5 h. The suspension was filtered with a glass pipette equipped with a cotton plug and washed successively with CH₂Cl₂ and Et₂O. The orange beads of the PS resin were dried under vacuum at 60 °C for 6 h, and analyzed by ³¹P CP/MAS NMR spectroscopy.

The Reaction of PS resin **3d** and [PdCl₂(PhCN)₂] (P/Pd 2:1, 1:2) (Figure S7).

The PS resin **3d** ([P] 0.08 mmol/g, 200 mg, 0.016 mmol) and [PdCl₂(PhCN)₂] (0.008 mmol for P/Pd 2:1, 0.032 mmol for P/Pd 1:2) were placed in a 5-mL vial tube. Anhydrous and degassed THF (2 mL) was added to the tube, and the mixture was

stirred at room temperature for 0.5 h. The suspension was filtered with a glass pipette equipped with a cotton plug and washed successively with CH₂Cl₂ and Et₂O. The orange beads of the PS resin were dried under vacuum at 60 °C for 6 h, and analyzed by ³¹P CP/MAS NMR spectroscopy.

The Reaction of PS resin 4 and [PdCl₂(PhCN)₂] (P/Pd 2:1, 1:2).

The PS resin **4** ([P] 0.07 mmol/g, 200 mg, 0.014 mmol) and [PdCl₂(PhCN)₂] (0.007 mmol for P/Pd 2:1, 0.028 mmol for P/Pd 1:2) were placed in a 5-mL vial tube. Anhydrous and degassed THF (2 mL) was added to the tube, and the mixture was stirred at room temperature for 0.5 h. The suspension was filtered with a glass pipette equipped with a cotton plug and washed successively with CH₂Cl₂ and Et₂O. The orange beads of the PS resin were dried under vacuum at 60 °C for 6 h, and analyzed by ³¹P CP/MAS NMR spectroscopy.

The Reaction of PS resin 5 and [PdCl₂(PhCN)₂] (P/Pd 2:1, 1:2).

The PS resin **5** ([P] 0.07 mmol/g, 200 mg, 0.014 mmol) and [PdCl₂(PhCN)₂] (0.007 mmol for P/Pd 2:1, 0.028 mmol for P/Pd 1:2) were placed in a 5-mL vial tube. Anhydrous and degassed THF (2 mL) was added to the tube, and the mixture was stirred at room temperature for 0.5 h. The suspension was filtered with a glass pipette equipped with a cotton plug, and washed successively with CH₂Cl₂ and Et₂O. The orange beads of the PS resin were dried under vacuum at 60 °C for 6 h, and analyzed by ³¹P CP/MAS NMR spectroscopy.

NMR Studies for the Reactions of the Soluble Ligand and Pd(II) Complexes

The Reaction of (*p*-Tol)₃P and [PdCl₂(PhCN)₂] (P/Pd 2:1, 1:1, 1:2) (Figure 8). [PdCl₂(PhCN)₂] (0.02 mmol) and (*p*-Tol)₃P (0.04 mmol for P/Pd 2:1, 0.02 mmol for P/Pd 1:1, 0.01 mmol for P/Pd 1:2) were placed in a 5-mL vial tube. Anhydrous and degassed CDCl₃ (0.7 mL) was added to the tube, and the mixture was stirred at room temperature for 0.5 h. The orange solution was analyzed by ³¹P NMR spectroscopy.

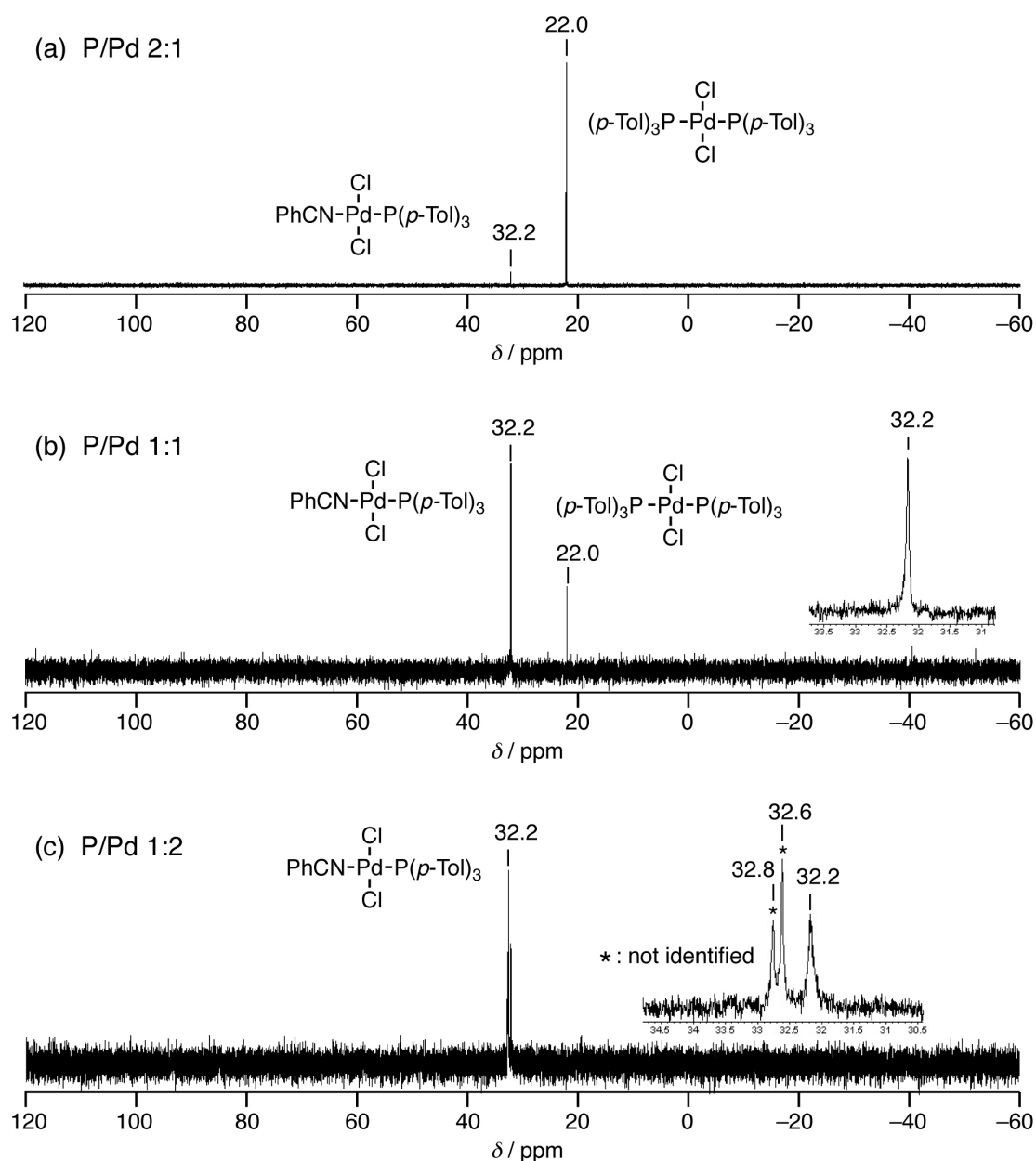


Figure 8. ^{31}P NMR spectra in CDCl_3 obtained after the reaction of $(p\text{-Tol})_3\text{P}$ and $[\text{PdCl}_2(\text{PhCN})_2]$ (P/Pd (a) 2:1, (b) 1:1 and (c) 1:2).

Reuse of Pd-3c for Suzuki–Miyaura Coupling between 6a and 7a (Figure 9–12)

In a glove box, PS resin **3c** ([P] 0.09 mmol/g, 224 mg, 0.02 mmol, 2 mol% P) was placed in a 10-mL glass tube containing a magnetic stirring bar. A solution of $[\{\text{PdCl}(\eta^3\text{-cinnamyl})\}_2]$ (2.6 mg, 0.005 mmol, 1 mol% Pd) in anhydrous and degassed THF (2 mL) was added to the tube. After stirring for 15 minutes, dibenzyl (internal standard for ^1H NMR analysis, 182 mg, 1 mmol), K_3PO_4 (636 mg, 3 mmol),

phenylboronic acid (**7a**, 183 mg, 1.5 mmol) and 4-chlorotoluene (**6a**, 127 mg, 1 mmol) were added successively. The tube was sealed with a screw cap and removed from the glove box. The reaction mixture was stirred at 60 °C for 2 h. A small aliquot (0.02 mL) was taken out from the reaction mixture on a timely base, and the yield of **8a** was determined by ^1H NMR analysis. The mixture was filtered through a glass pipette equipped with a cotton plug. The inorganic salts were removed by washing with H_2O , and then solvent displacement was performed with THF followed by Et_2O . After drying under vacuum, the recovered insoluble catalyst was placed in the vial tube that was used for the second run. Anhydrous, degassed THF (2 mL), dibenzyl (internal standard, 182 mg, 1 mmol), K_3PO_4 (636 mg, 3 mmol), phenylboronic acid (**7a**, 183 mg, 1.5 mmol) and 4-chlorotoluene (**6a**, 127 mg, 1 mmol) were added, and the mixture was stirred at 60 °C for 2 h. The yield of **8a** was determined by ^1H NMR analysis. This reusing procedure was repeated seven times (1st use, 91%; 2nd use, 97%; 3rd use, 98%; 4th use, 94%; 5th use, 85%; 6th use, 70%; 7th use, 47%; 8th use, 24%; Figure 9).

The recovered Pd-**3c** resins after the 8th run was reused for the 9th run with a reload of $[\{\text{PdCl}(\eta^3\text{-cinnamyl})\}_2]$ (2.6 mg, 0.005 mmol, 1 mol% Pd). A time–yield profile is shown in Figure S16 (black filled squares; 0.5 h, 29%; 1 h, 48%; 1.5 h, 61%; 2 h, 64%; 3 h, 75%; 4 h 76%).

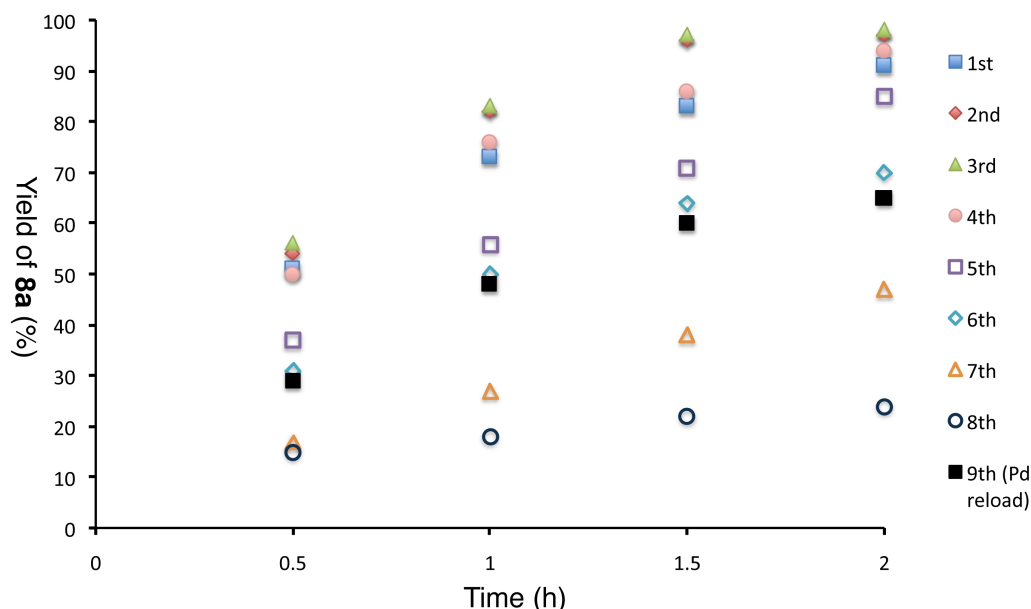
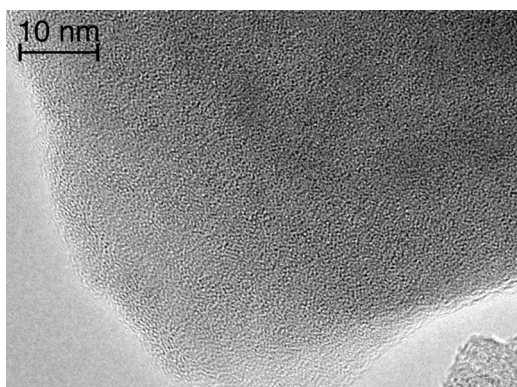


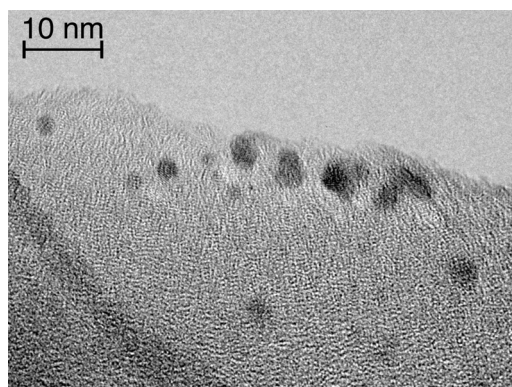
Figure 9. Time–yield profiles for the reaction of **6a** and **7a** with the Pd-**3c** system.

The HR-TEM images of the Pd-**3c** resins after the 1st, 4th and 8th runs are shown in Figure 10.

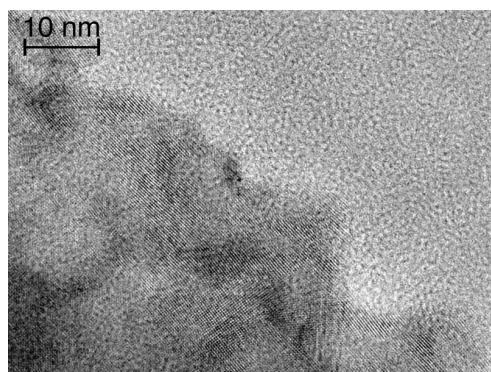
a) 1st run



b) 4th run



c) 8th run



d) 8th run

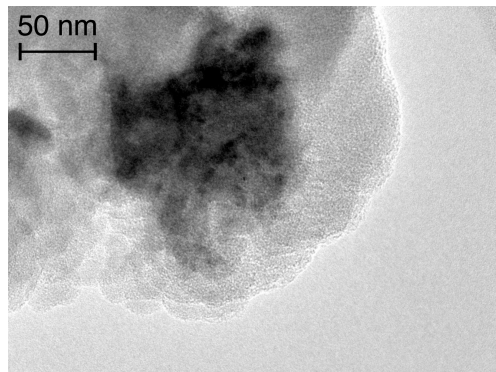


Figure 10. HR-TEM images of part of the Pd-**3c** resins after (a) 1st, (b) 4th and (c,d) 8th runs, respectively.

The ^{31}P CP/MAS spectrum of the Pd-**3c** resins after the 8th run is shown in Figure 11. This spectrum looks similar to that obtained by treating **3c** with $\text{Pd}(\text{dba})_2$ (dba: dibenzalacetone, P/Pd 2:1, THF, r.t. 1 h, Figure S4): part of Pd remained in solution as judged by the color of the supernatant solution.

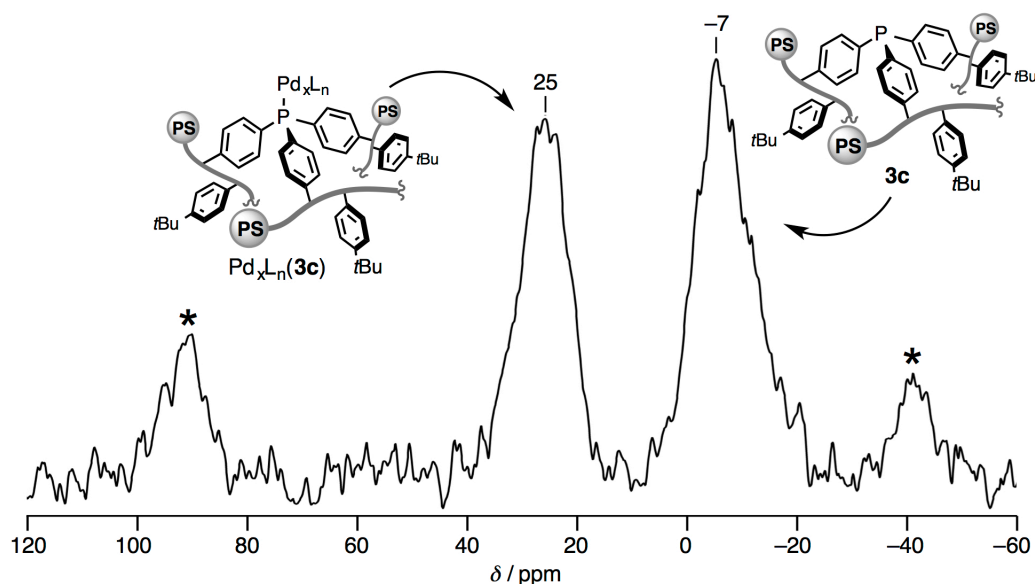


Figure 11. ^{31}P CP/MAS NMR spectrum of the Pd-**3c** resin taken after 8th catalytic run. Asterisks(*) indicate spinning side bands.

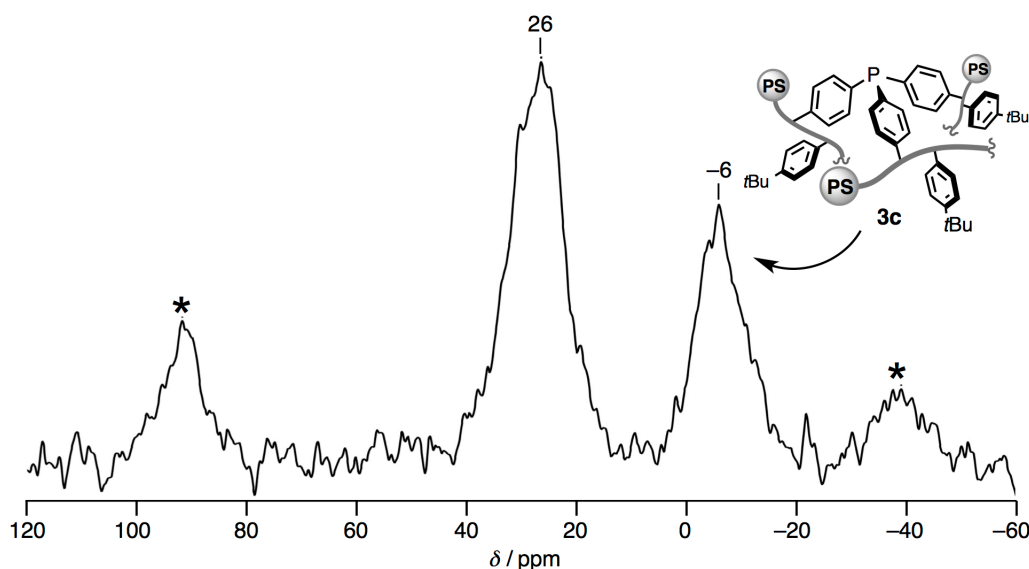
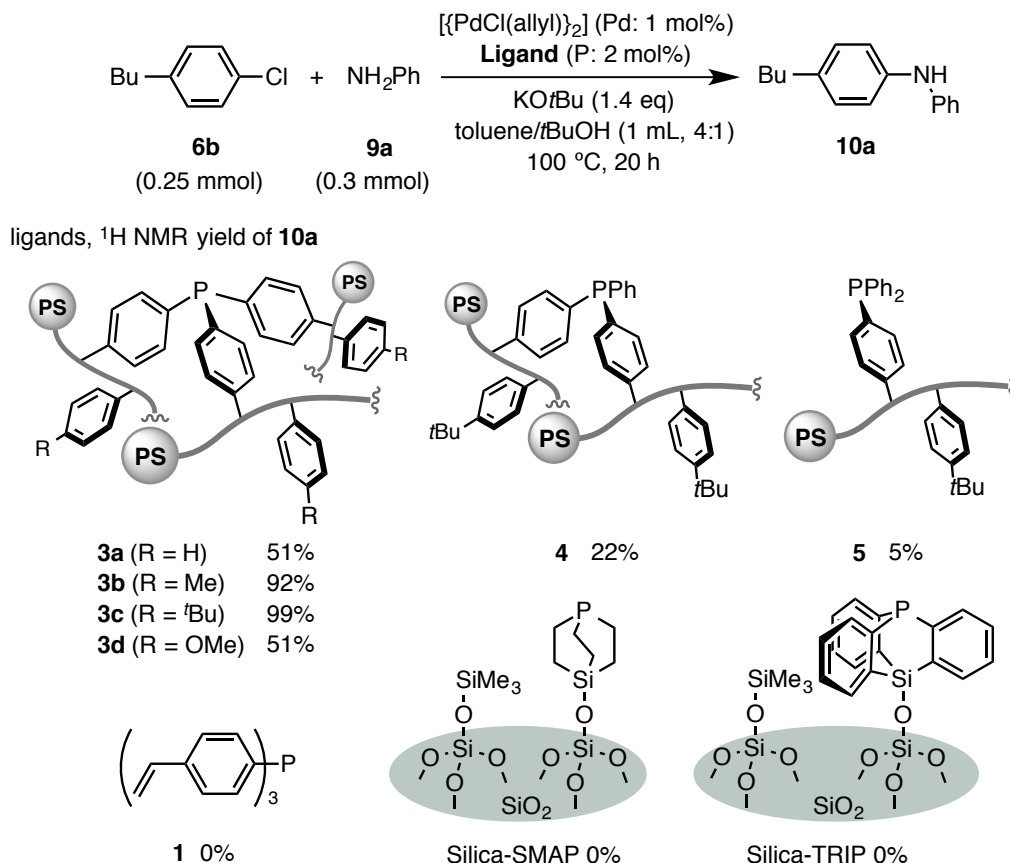


Figure 12. ^{31}P CP/MAS NMR spectrum obtained after the reaction of **3c** and $[\text{Pd}(\text{dba})_2]$ (P/Pd 2:1). Asterisks(*) indicate spinning side bands.

Ligand Effects in the Pd-Catalyzed Amination of Chloroarene **6b** with **9a** (Scheme 4)

Scheme 4. Ligand Effects for Pd-Catalyzed Amination of **6b** with **9a**.



Typical Procedures for Transition Metal Catalysis

Pd-Catalyzed Suzuki–Miyaura Cross-Coupling Reaction (Scheme 2).

In a glove box, PS resin **3c** ([P] 0.09 mmol/g, 112 mg, 0.01 mmol, 2 mol% P) was placed in a 10-mL glass tube containing a magnetic stirring bar. A solution of $[\text{PdCl}_2(\text{PhCN})_2]$ (1.9 mg, 0.005 mmol, 1 mol% Pd) in anhydrous and degassed THF (1 mL) was added to the tube. After stirring for 5 minutes, K_3PO_4 (318 mg, 1.5 mmol), phenylboronic acid (**7a**, 91.4 mg, 0.75 mmol) and 4-chlorotoluene (**6a**, 63.3 mg, 0.5 mmol) were added successively. The tube was sealed with a screw cap and removed from the glove box. The reaction mixture was stirred at 40 °C for 2 h, and then filtered through a glass pipette equipped with a cotton plug. Solvent was removed under reduced pressure. An internal standard (1,1,2,2-tetrachloroethane) was added to determine the yield of the product by ¹H NMR (95%). The crude material was then

purified by silica gel chromatography to give biaryl **8a** (71.2 mg, 0.43 mmol, 85% yield).

Pd-Catalyzed Amination of Chloroarene (Table 2).

In a glove box, the PS resin **3c** ([P] 0.09 mmol/g, 84 mg, 0.0075 mmol, 3 mol% P) was placed in a 10-mL glass tube containing a magnetic stirring bar. A solution of [$\{\text{PdCl}(\eta^3\text{-allyl})\}_2$] (0.69 mg, 0.0019 mmol, 1.5 mol% Pd) in anhydrous and degassed toluene (0.8 mL) were added to the tube. After stirring for 5 minutes, anhydrous, degassed $t\text{-BuOH}$ (0.2 mL), KO^tBu (39.3 mg, 0.35 mmol), *p*-butylchlorobenzene (**6b**, 42.2 mg, 0.25 mmol), and aniline (**9a**, 27.9 mg, 0.3 mmol) were added successively. The tube was sealed with a screw cap and removed from the glove box. The reaction mixture was stirred at 100 °C for 20 h, and filtered with a Celite[®] pad. The solvent was removed under reduced pressure. An internal standard (1,1,2,2-tetrachloroethane) was added to the residue. The yield of the product was determined by ^1H NMR (99%). The crude material was then purified by silica gel chromatography (90:10 hexane/EtOAc) to give the diarylamine **10a** (45.1 mg, 80% yield).

Ir-Catalyzed C(sp³)-H Borylation (Table 1).

In a glove box, the PS resin **3c** ([P] 0.09 mmol/g, 67 mg, 0.006 mmol, 2 mol% P) and bis(pinacolato)diboron (**12**, 76.2 mg, 0.3 mmol) were placed in a 10-mL glass tube containing a magnetic stirring bar. A solution of [$\{\text{Ir}(\text{OMe})(\text{cod})\}_2$] (2 mg, 0.003 mmol, 2 mol% Ir) in anhydrous, degassed CPME (1 mL) and 2-penthyropyridine (**11**) (96.4 mg, 0.9 mmol) were added successively. The tube was sealed with a screw cap and removed from the glove box. The reaction mixture was stirred at 60 °C for 15 h, and then filtered through a glass pipette equipped with a cotton plug. The solvent was removed under reduced pressure. An internal standard (1,1,2,2-tetrachloroethane) was added to the residue. The yield of the product was determined by ^1H NMR (82% yield based on **12**). The crude material was then purified by Kugelrohr distillation to give the corresponding product **13** (34.7 mg, 42% yield based on **12**).

Rh-Catalyzed N-Adjacent C(sp³)-H Borylation (Scheme 3, upper).

In a glove box, the PS resin **3c** ([P] 0.09 mmol/g, 27.8 mg, 0.0025 mmol P, 1 mol% P), bis(pinacolato)diboron (**12**, 63.5 mg, 0.25 mmol) were placed in a 10-mL glass tube

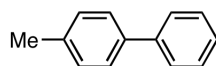
containing a magnetic stirring bar. A solution of [$\{\text{Rh}(\text{OMe})(\text{cod})\}_2$] (0.6 mg, 0.0012 mmol, 1 mol% Rh) in anhydrous, degassed THF (0.5 mL) and *N,N'*-dimethylpropyleneurea (**14**, 64.1 mg, 0.5 mmol) were added successively to the tube. The tube was sealed with a screw cap, and was removed from the glove box. The mixture was stirred at 70 °C for 6 h, and then filtered through a glass pipette equipped with a cotton plug. Solvent was removed under reduced pressure. An internal standard (1,1,2,2-tetrachloroethane) was added to determine the yield of the product by ^1H NMR (73% yield based on B atom). The crude material was then purified by Kugelrohr distillation to give the corresponding product **15** (79.6 mg, 0.31 mmol, 63% yield based on B atom).

Rh-Catalyzed N-Adjacent C(sp³)-H Borylation (Scheme 3, bottom).

In a glove box, the PS resin **3c** ([P] 0.09 mmol/g, 27.8 mg, 0.0025 mmol P, 1 mol% P), bis(pinacolato)diboron (**12**, 63.5 mg, 0.25 mmol) were placed in a 10-mL glass tube containing a magnetic stirring bar. A solution of [$\{\text{Rh}(\text{OMe})(\text{cod})\}_2$] (0.6 mg, 0.0012 mmol, 1 mol% Rh) in anhydrous, degassed hexane (0.5 mL) and 2-(piperidin-1-yl)pyridine (**16**, 81.1 mg, 0.5 mmol) were added successively to the tube. The tube was sealed with a screw cap, and was removed from the glove box. The mixture was stirred at 80 °C for 15 h, and then filtered through a glass pipette equipped with a cotton plug. Solvent was removed under reduced pressure. An internal standard (1,1,2,2-tetrachloroethane) was added to determine the yield of the product by ^1H NMR (90% yield based on B atom). The crude material was then purified by Kugelrohr distillation to give the corresponding product **17** (129 mg, 0.45 mmol, 89% yield based on B atom).

12. Characterization of Products

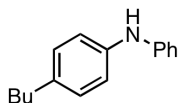
4-Methyl-1,1'-biphenyl (**8a**)^[28]



Isolated by silica gel chromatography with hexane (71.2 mg, 85% yield).

^1H NMR (CDCl_3): δ 2.40 (s, 3H), 7.22–7.28 (m, 2H), 7.28–7.37 (m, 1H), 7.38–7.47 (m, 2H), 7.48–7.54 (m, 2H), 7.55–7.62 (m, 2H). ^{13}C NMR (CDCl_3): δ 20.95, 127.03 (3C), 127.05 (2C), 128.77 (2C), 129.54 (2C), 137.08, 138.44, 141.25.

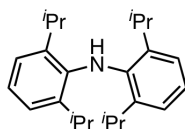
4-Butyl-*N*-phenylaniline (10a)^[29]



Isolated by silica gel chromatography with 90:10 hexane/EtOAc (45.1 mg, 80% yield).

¹H NMR (CDCl₃): δ 0.93 (t, *J* = 7.5 Hz, 3H), 1.30–1.43 (m, 2H), 1.50–1.64 (m, 2H), 2.56 (t, *J* = 7.5 Hz, 2H), 5.61 (s, 1H), 6.84–6.91 (m, 1H), 6.99–7.11 (m, 5H), 7.21–7.27 (m, 3H). ¹³C NMR (CDCl₃): δ 13.86, 22.23, 33.73, 34.83, 116.97 (2C), 118.72 (2C), 120.34, 129.27 (2C), 129.36 (2C), 136.12, 140.54, 143.95.

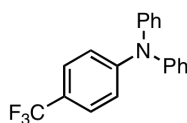
Bis(2,6-diisopropylphenyl)amine (10b)^[30]



Isolated by silica gel chromatography with 90:10 hexane/EtOAc (67.5 mg, 80% yield).

¹H NMR (CDCl₃): δ 1.08 (d, *J* = 6.9 Hz, 24H), 3.08 (sep, *J* = 6.9 Hz, 4H), 4.89 (s, 1H), 7.00–7.13 (m, 6 H). ¹³C NMR (CDCl₃): δ 23.43 (8C), 27.64 (4C), 122.80 (2C), 123.89 (4C), 140.48 (2C), 140.93 (4C).

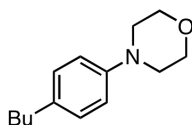
***N,N*-Diphenyl-4-(trifluoromethyl)aniline (10c)**^[31]



Isolated by silica gel chromatography with hexane (58.0 mg, 75% isolated).

¹H NMR (CDCl₃): δ 7.03–7.14 (m, 7H), 7.25–7.34 (m, 5H) 7.42 (d, *J* = 9.0 Hz, 2H). ¹³C NMR (CDCl₃): δ 121.09 (2C), 122.86 (q, *J*_{C-F} = 32.5 Hz), 124.29 (2C), 124.57 (q, *J*_{C-F} = 270.0 Hz), 125.56 (4C), 126.32 (q, *J*_{C-F} = 3.4 Hz, 2C), 129.66 (4C), 146.95 (2C), 151.03.

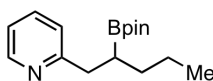
4-(4-Butylphenyl)morpholine (10d)^[33]



Isolated by silica gel chromatography with hexane (36.7 mg, 67% yield).

¹H NMR (CDCl₃): δ 0.91 (t, *J* = 7.5 Hz, 3H), 1.27–1.40 (m, 2H), 1.51–1.62 (m, 2H), 2.54 (t, *J* = 7.8 Hz, 2H), 3.10–3.14 (m, 4H), 3.84–3.88 (m, 4H), 6.82–6.88 (m, 2H), 7.08–7.12 (m, 2H). **¹³C NMR** (CDCl₃): δ 13.83, 22.21, 33.70, 34.58, 49.71 (2C), 66.96 (2C), 115.90 (2C), 129.13 (2C), 134.73, 149.38.

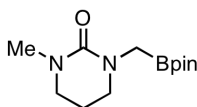
2-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)pyridine (13)^[22f]



Isolated by Kugelrohr distillation (34.7 mg, 42% yield).

¹H NMR (CDCl₃): δ 0.88 (t, *J* = 7.1 Hz, 3H), 1.12–1.19 (m, 2H), 1.23 (s, 6H), 1.24 (s, 6H), 1.30–1.40 (m, 2H), 1.42–1.55 (m, 1H), 2.82 (dd, *J* = 16.2, 6.6 Hz, 1H), 3.07 (dd, *J* = 16.2, 6.6 Hz, 1H), 7.22 (t, *J* = 6.3 Hz, 1H), 7.27 (d, *J* = 7.7 Hz, 1H), 7.70 (td, *J* = 7.7, 1.5 Hz, 1H), 8.54 (d, *J* = 5.1 Hz, 1H). **¹³C NMR** (CDCl₃): δ 14.26, 22.24, 25.49 (2C), 25.58 (2C), 33.28, 38.13, 80.92 (2C), 121.64, 123.47, 138.39, 144.93, 162.72. A signal for the carbon directly attached to the boron atom was not observed.

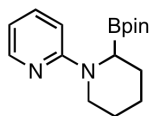
1-Methyl-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)tetrahydropyrimidin-2(1H)-one (15)^[23]



Isolated by Kugelrohr distillation (79.6 mg, 63% based on B atom).

¹H NMR (CDCl₃): δ 1.19 (s, 12H), 1.96 (quint, *J* = 5.7 Hz, 2H), 2.35 (s, 2H), 2.98 (s, 3H), 3.21–3.26 (m, 4H). **¹³C NMR** (CDCl₃): δ 20.72, 24.95 (4C), 35.82, 42.21 (br), 44.49, 46.40, 79.44 (2C), 159.60.

2-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)piperidin-1-yl)pyridine (17)^[23]



Isolated by Kugelrohr distillation (129 mg, 89% based on B atom).

¹H NMR (CDCl₃): δ 1.18–1.30 (m, 12H), 1.41–1.49 (m, 3H), 1.68–1.72 (m, 1H), 1.76–1.81 (m, 1H), 1.86 (m, 1H), 2.37 (d, *J* = 12.0 Hz, 1H), 2.99 (tm, *J* = 12.6 Hz, 1H), 3.70 (d, *J* = 12.0 Hz, 1H), 6.36–6.45 (m, 2H), 7.44 (tm, *J* = 6.0 Hz, 1H), 7.91 (d, *J* = 6.0 Hz, 1H). **¹³C NMR** (CDCl₃): δ 25.06, 25.66, 25.85–26.59 (br-m, 4C), 26.96, 43.56, 52.84 (br), 78.89 (2C), 105.33, 109.15, 139.47, 141.04, 156.14.

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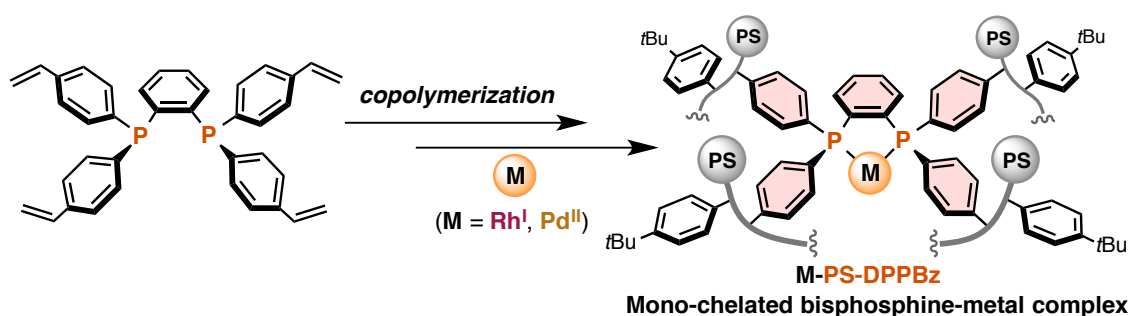
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- [16] Experiments with an excess amount of chloroarene (**6a**; 1.5 mmol, **7a**; 1 mmol) under otherwise identical conditions resulted in decreased catalytic efficacies (yield of **8a**: 1st, 66%; 2nd, 86%; 3rd, 75%; 4th, 76%).
- [17] A hot filtration test of the Pd-**3c** catalyst indicated that no meaningful reaction occurred in the solution phase.
- [18] HR-TEM observation after the 8th run (**8a**; 24% yield, 2 h) indicated the formation of larger Pd aggregates. See Experimental Section for other HR-TEM images (Figure 10) and the ³¹P CP/MS spectrum of the regins after the 8th run (Figure 11). The Pd cluster formation occurred likely via dissociation of the Pd from the P atom.
- [19] ICP-AES analyses indicated that Pd (Scheme 3), Rh (Scheme 4) and Ir (Table 1) in the solution pase after the reaction were <0.02%, 3.6% and <0.02% of the loaded metals, respectively.
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Chapter 2

Development of Bisphosphine-Branched Polystyrene; Synthesis and Coordination Property toward Transition-Metal Complexes



Abstract

A bisphosphine-branched polystyrene PS-DPPBz was synthesized through radical emulsion copolymerization of 4-*t*-butylstyrene in the presence of tetravinylated 1,2-bis(diphenylphosphino)benzene as a fourfold cross-linker. The ^{31}P CP/MAS NMR studies for the coordination behavior of the PS-DPPBz ligand toward Rh(I) and Pd(II) complexes showed the mono-ligating property. The rigid *o*-phenylene scaffold to connect two P atoms is critical for the chelate coordination in the polymer matrix.

Introduction

Bisphosphines are common and useful bidentate ligands for transition-metal catalysts. Owing to the strong coordination ability toward metals by chelation, immobilization of bisphosphines onto a solid support has been widely studied for preparation of heterogenized transition-metal catalysts. However, such immobilized ligands often decreased their performance compared to homogeneous counterparts due to unfavorable steric effects of the solid support toward the catalytic site.

To overcome these problems, the author designed and synthesized a new type of a monophosphine-branched polystyrene PS-TPP, as described in Chapter 1.² Owing to the effective site isolation of the P center by the threefold-cross-linking, PS-TPP allowed the selective formation of catalytically active metal-P 1:1 species with minimal steric hindrance from the polymer support (Figure 1a). Accordingly, PS-TPP showed excellent ligand performances in challenging metal catalysis, irrespective of moderate electronic and steric natures of the PPh₃-based ligand.

On the basis of this knowledge, the author envisaged that the concept of the polymer cross-linking by phosphine could expand to bisphosphines for construction of efficient heterogeneous bisphosphine-metal catalyst systems. To this end, 1,2-bis(diphenylphosphino)benzene (DPPBz) would be a suitable motif for the bisphosphine-branched polystyrene. The rigid *o*-phenylene scaffold of DPPBz allows the two P atoms to maintain *cis* conformation even in the flexible polymer matrix, resulting in effective formation of chelating bisphosphine-metal 1:1 species (Figure 1b).

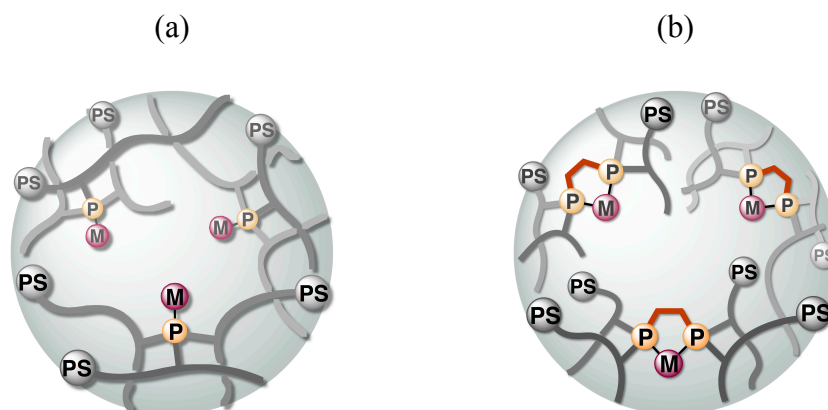


Figure 1. Conceptual views of metal complexes (a) with a threefold cross-linked PS-monophosphine hybrid (ref 5.) and (b) with a bisphosphine-branched polystyrene (This work).

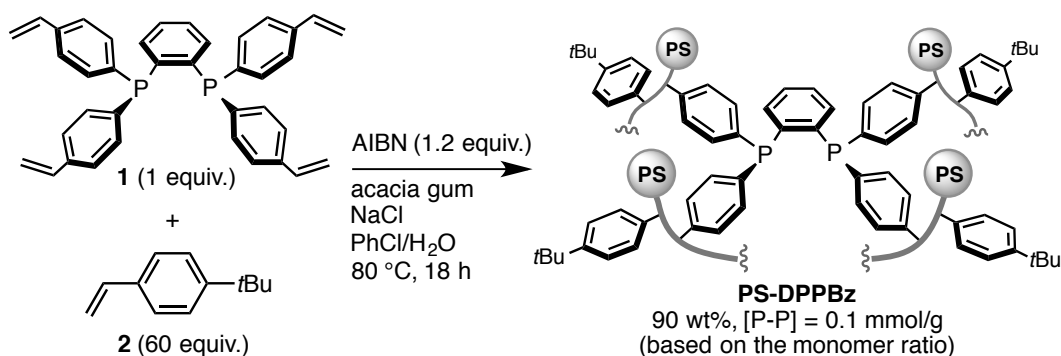
In this chapter, the author describes the synthesis of the PS-DPPBz, bisphosphine-branched polystyrene bearing a 1,2-bis(diphenylphosphino)benzene core. The mono-ligating property of PS-DPPBz toward Rh(I) and Pd(II) complexes were demonstrated by the ^{31}P CP MAS NMR analysis.

Results and Discussion

Ligand Synthesis and Characterization

Synthesis of a bisphosphine-branched polystyrene with a DPPBz core was shown in Scheme 1. Radical emulsion polymerization of 4-*t*-butylstyrene (**2**, 60 equiv) in the presence of tetravinylated DPPBz (**1**)³⁻⁶ as a cross-linker gave PS-DPPBz in 90 wt% yield as bead-shaped insoluble materials. The obtained beads of PS-DPPBz showed ordinary swelling properties as PS resin for common organic solvents. The ^{31}P CP/MAS NMR spectrum of the dried PS-DPPBz exhibited a broad signal at $\delta -17$ (ppm) (Figure 2a), indicating that their electronic and steric properties are virtually same as that of a DPPBz molecule [^{31}P NMR (CDCl_3); $\delta -13$]. In the ^{13}C CP/MAS spectrum, no signal derived from vinyl groups around $\delta 115$ suggested successful fourfold cross-linking of polystyrene by the DPPBz core (Figure 2b). Thus, the loading of DPPBz moiety to the polymer matrix was calculated to be 0.10 mmol/g on the assumption that all vinyl substrates were completely polymerized. This value was comparable to the estimated value by combustion elemental analysis on P (0.12 mmol/g).

Scheme 1. Synthesis of PS-DPPBz



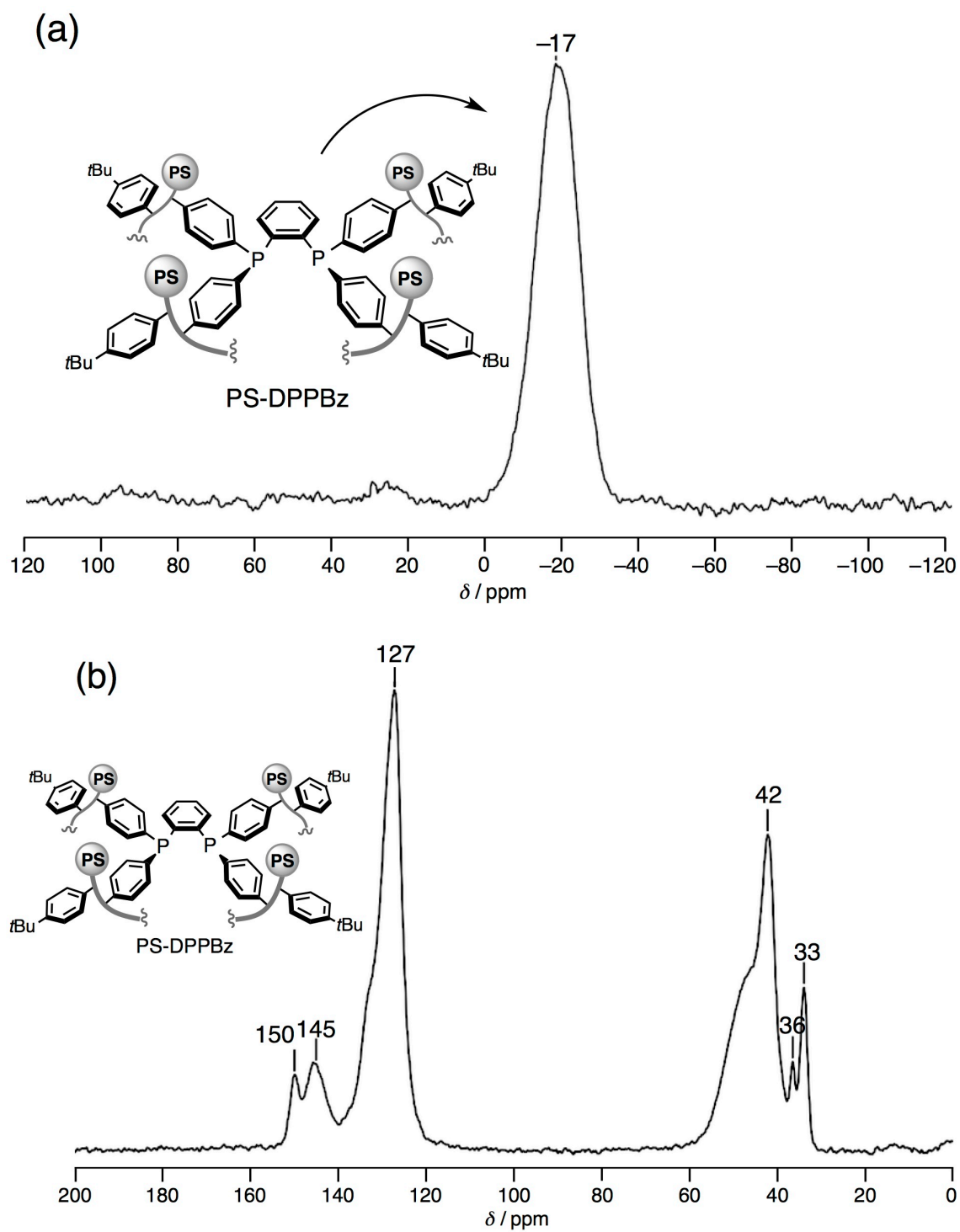


Figure 2. (a) ^{31}P CP/MAS and (b) ^{13}C CP/MAS spectra of PS-DPPBz.

Coordination property of PS-DPPBz toward a cationic Rh complex

The coordination property of PS-DPPBz toward a cationic Rh(I) complex was investigated. Specifically, the reaction of PS-DPPBz with $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (PS-DPPBz/Rh 1:1) was conducted in CH_2Cl_2 at room temperature. After filtration, washing and drying, the solid-state ^{31}P CP/MAS NMR of the yellow beads gave a signal of the 1:1 Rh/PS-DPPBz complex $[\text{Rh}(\text{cod})(\text{PS-DPPBz})]\text{BF}_4$ at δ 53 (Figure 3a), indicating that almost all of the bisphosphine moiety were accessible for the metal complexation. Even with excess bisphosphine toward the Rh(I) complex, the mono-ligating Rh(I) complex was formed selectively (Figure 3b). In contrast, the reaction of $[\text{Rh}(\text{cod})_2]\text{BF}_4$ with the soluble ligand DPPBz (1:1 Rh/DPPBz) at room temperature afforded a mixture of 1:1 Rh/DPPBz complex $[\text{Rh}(\text{cod})(\text{DPPBz})]\text{BF}_4$ and 1:2 Rh/DPPBz complex $[\text{Rh}(\text{DPPBz})_2]\text{BF}_4$ at δ 62.8 and δ 57.8, respectively (Figure 4a). When excess bisphosphine was present (1:2 Rh/DPPBz), only the 1:2 Rh/DPPBz complex $[\text{Rh}(\text{DPPBz})_2]\text{BF}_4$ was formed (Figure 4b). These results indicated that bisphosphine-cross-linking into the polymer matrix is an effective way to realize site isolation of the coordination center.

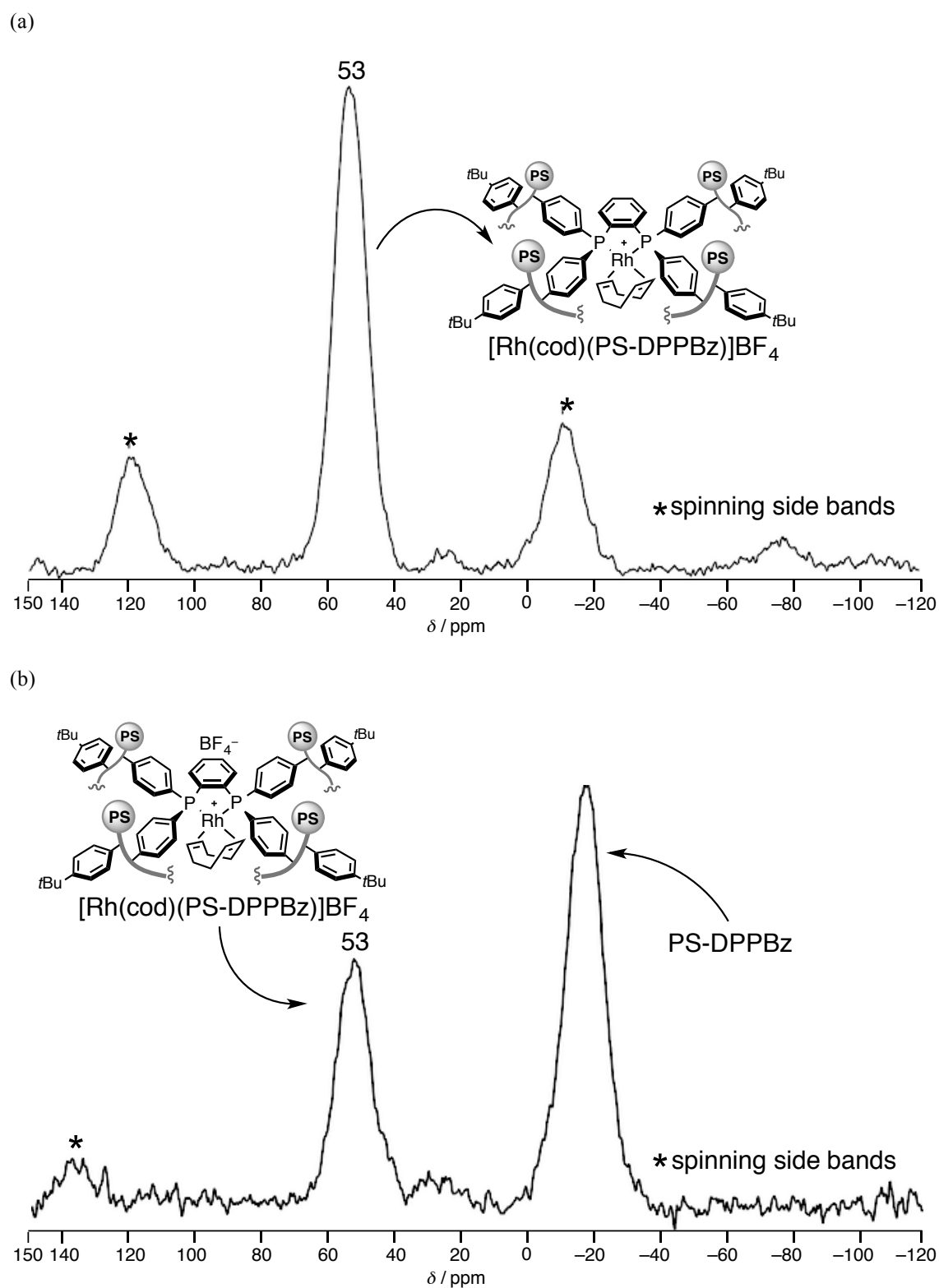


Figure 3. ^{31}P CP/MAS spectrum obtained from $[\text{Rh}(\text{cod})_2]\text{BF}_4$ and PS-DPPBz [(a)1:1 Rh/ PS-DPPBz, (b) 1:2 Rh/PS-DPPBz]

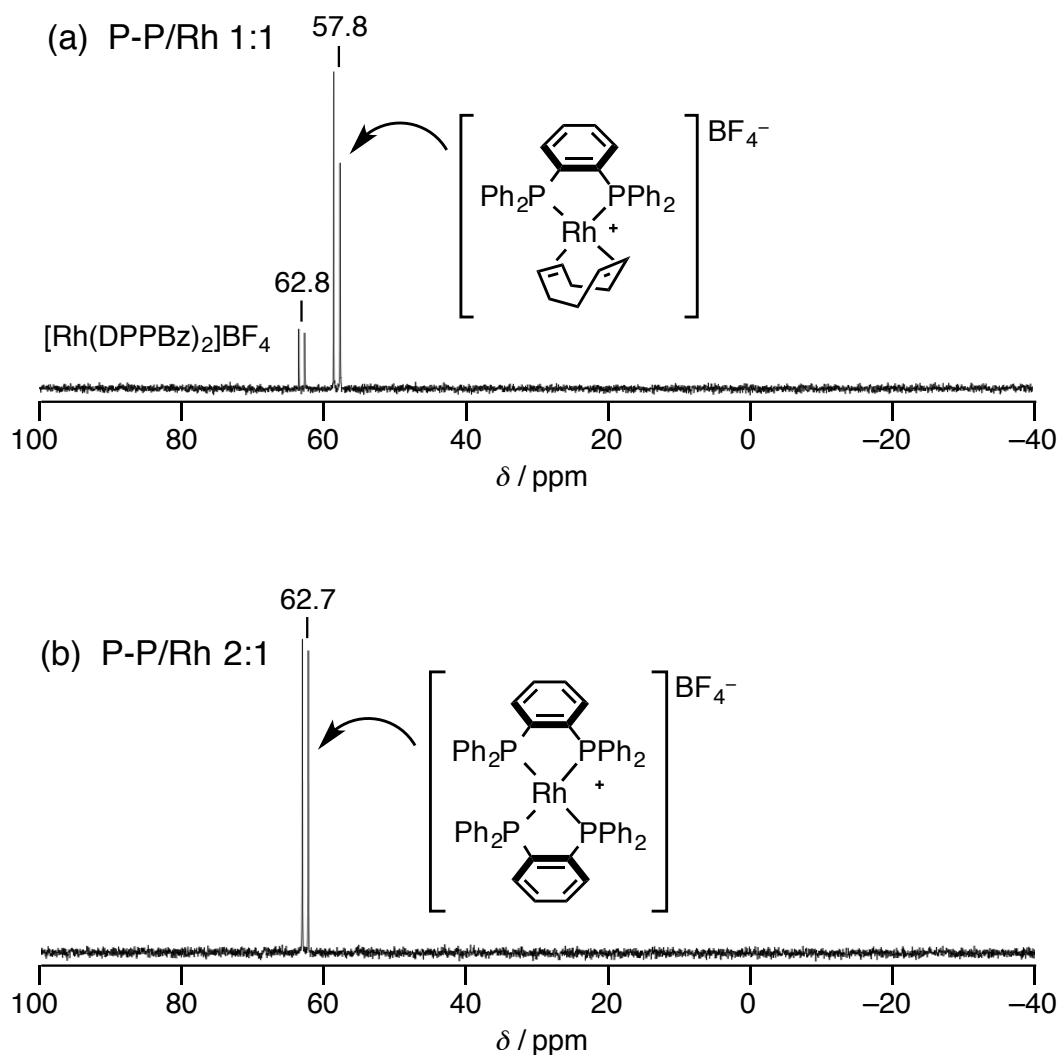


Figure 4. ^{31}P spectrum in CDCl_3 obtained from $[\text{Rh}(\text{cod})_2]\text{BF}_4$ and homogeneous DPPBz [(a)1:1 Rh/ DPPBz, (b) 1:2 Rh/ DPPBz]

Coordination property with Pd complex

Next, the reaction of $\text{PdCl}_2(\text{cod})$ with PS-DPPBz were conducted in THF at room temperature (2:1 Pd/PS-DPPBz). As shown in Figure 5a, only a signal at $\delta 60$, which was assignable to the 1:1 Pd/P complex $\text{PdCl}_2(\text{PS-DPPBz})$ on the basis of the ^{31}P NMR study using the homogeneous DPPBz ligand, was observed exclusively, again indicating successful chelate coordination of DPPBz core toward metal in the polymer matrix.

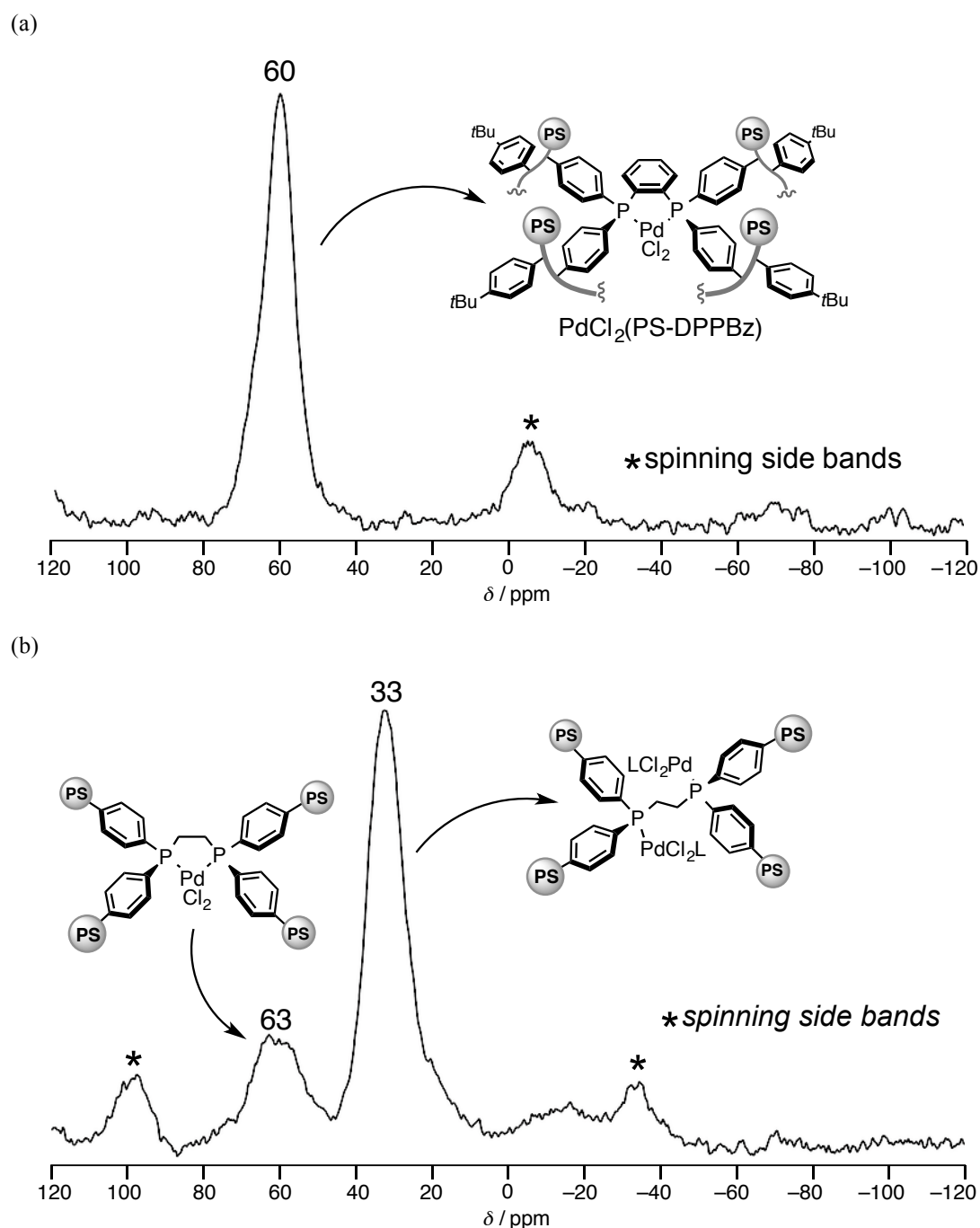


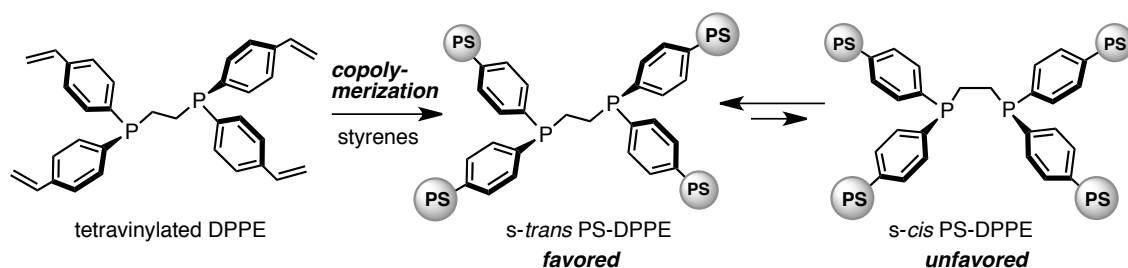
Figure 5. ^{31}P CP/MAS spectrum obtained (a) for $\text{PdCl}_2(\text{cod})$ and PS-DPPE (2:1 Pd/PS-DPPBz) and (b) for $\text{PdCl}_2(\text{cod})$ and PS-DPPE (2:1 Pd/PS-DPPE).

In contrast, a fourfold polystyrene-cross-linking 1,2-bis(diphenylphosphino)ethane-based ligand PS-DPPE, which was prepared from tetravinylated DPPE and 4-*t*-butylstyrene through the radical emulsion polymerization

method, gave two separated signals at δ 33 and δ 63 (Figure 5b), which corresponds to a mono-P-ligated palladium complex **A** and a monochelate 1:1 Pd/bisphosphine complex **B**, respectively, on the basis of ^{31}P NMR studies using homogenous counterparts such as DPPE and PPh_2Me .

The difference of the coordination properties between PS-DPPBz and PS-DPPE demonstrated the importance of the linker to connect two P atoms for better metal chelation. The rigid *o*-phenylene scaffold of the DPPBz core allowed the two P atoms in the *cis* conformation even after copolymerization. On the other hand, more flexible ethylene linker of the DPPE core is unfavorable for the chelate coordination in the polymer matrix. This is because the direction of the two P atoms was kept fixed in *trans* conformation after polymerization (Scheme 2).

Scheme 2. The *s-trans* and *s-cis* forms of PS-DPPBz



Conclusion

A new bisphosphine-branched polystyrene PS-DPPBz was synthesized through radical emulsion polymerization of 4-*t*-butylstyrene with tetravinylated 1,2-bis(diphenylphosphino)benzene as a fourfold cross-linker. The coordination studies toward transition-metal complexes by ^{31}P CP/MAS NMR analysis revealed two important things for polymer effects to bisphosphines. Firstly, the multifold crosslinking by bisphosphine enables site isolation of each coordination site, resulting in selective formation of 1:1 metal-bisphosphine complexes. Secondly, the rigid *o*-phenylene scaffold of the DPPBz core is favorable to maintain the two P atoms in *cis* conformation for better metal chelation. Owing to these characteristic features, the PS-DPPBz would act as an effective heterogeneous ligand for transition-metal catalysis.

Experimental Section

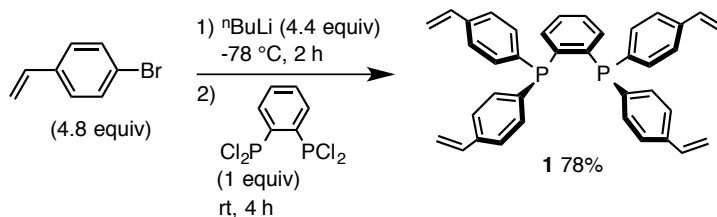
Instrumentation and Chemicals

Solution NMR spectra were recorded on a JEOL ECX-II (400 MHz for ^1H NMR, 100.5 MHz for ^{13}C NMR, and 161.8 MHz for ^{31}P NMR). Chemical shift values are referenced to Me_4Si (^1H), the residual solvent (^{13}C), and H_3PO_4 (^{31}P). Magic angle spinning (MAS) NMR spectra were recorded on a Bruker MSL-300 spectrometer, operating at 75.5 MHz for ^{13}C NMR, and 121.5 MHz for ^{31}P NMR. High-resolution mass spectra (Thermo Scientific Exactive or JEOL JMS-T100LC for ESI-MS, and JEOL JMS-T100GCv for EI-MS) were recorded at the Instrumental Analysis Division, Equipment Management Center, Creative Research Institution, Hokkaido University. Elemental analysis were performed at Center for Organic Elemental Microanalysis, Graduate School of Pharmaceutical Science, Kyoto University. ICP-AES analyses (Shimadzu ICPE-9000) were performed at Hokkaido University Sousei Hall. A microwave digestion system (Milestone, ETHOS One) was used to prepare samples for ICP-AES analysis. GLC analyses were conducted on a Shimadzu GC-14B equipped with a flame ionization detector. Melting points were determined on a micro melting point apparatus using micro cover glass (Yanaco MP-500D). TLC analyses were performed on commercial glass plates bearing 0.25 mm layer of Merck Silica gel 60F₂₅₄. Silica gel (Kanto Chemical Co., Ltd., Silica gel 60 N, spherical, neutral) was used for column chromatography.

All reactions were carried out under nitrogen or argon atmosphere. Materials were obtained from commercial suppliers or prepared according to standard procedures unless otherwise noted. 1,2-Bis(dichlorophosphino)benzene was purchased from Wako Pure Chemical Industries, Ltd. 1,2-Bis(dichlorophosphino)ethane was purchased from Aldrich Co., Ltd. *p-t*-Bu-styrene was purchased from TCI Co., Ltd., and purified by passing through a alumina column. Acacia [Gum Arabic] was purchased from Nacalai Tesque. $[\text{Rh}(\text{cod})_2]\text{BF}_4$, $\text{PdCl}_2(\text{cod})$ were prepared according to the literature.

2. Preparation of Bisphosphine monomers

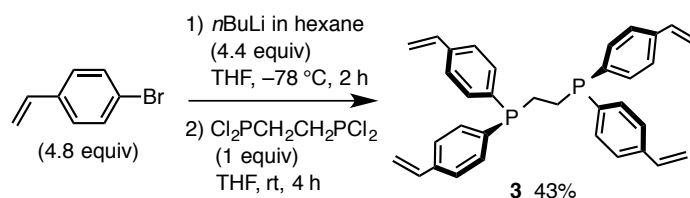
1,2-Bis(bis(4-vinylphenyl)phosphino)benzene (1)



In a 300-mL round-bottom flask equipped with a magnetic stirring bar, a solution of *n*-BuLi in hexane (1.6 M, 9.8 mL, 15.7 mmol, 4.4 equiv) was slowly added to the solution of 4-bromostyrene (3.1 g, 17 mmol, 4.8 equiv) in THF (65 mL) at $-78\text{ }^{\circ}\text{C}$. After the mixture was stirred for 2 h at $-78\text{ }^{\circ}\text{C}$, a solution of 1,2-bis(dichlorophosphino)benzene (1.0 g, 3.6 mmol) in THF (4 mL) was added at this temperature over 5 min. The mixture was warmed to room temperature and stirred for 4 h. After quenching with aq. NH_4Cl , the mixture was extracted with CH_2Cl_2 . The organic layer was washed with water, dried over MgSO_4 , filtered and concentrated. The residue was purified by silica gel chromatography (97:3 hexane/EtOAc) to give **4** as white solids (1.54 g, 78% yield).

White solids. M.p.: $69\text{--}71\text{ }^{\circ}\text{C}$. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 5.23 (d, $J = 11.2\text{ Hz}$, 4H), 5.72 (d, $J = 18.0\text{ Hz}$, 4H), 6.64 (dd, $J = 11.2, 18.0\text{ Hz}$, 4H), 7.08–7.13 (m, 10H), 7.19–7.27 (m, 10H). $^{13}\text{C NMR}$ (100.5 MHz, CDCl_3): δ 114.42 (s, 4C), 126.07 (m, 8C), 129.08 (s, 2C), 133.50–134.35 (m, 10C), 136.43 (s, 4C), 136.44 (s, 4C), 137.59 (s, 4C), 143.57 (t, $J = 10\text{ Hz}$, 2C). $^{31}\text{P NMR}$ (161.8 MHz, CDCl_3): δ -14.4 . IR (ATR) 754, 830, 907, 987, 1392, 1494, 1627 cm^{-1} . HRMS-EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{38}\text{H}_{32}\text{P}_2$, 550.19792; found, 550.19617.

1,2-Bis(bis(4-vinylphenyl)phosphino)ethane (**3**)

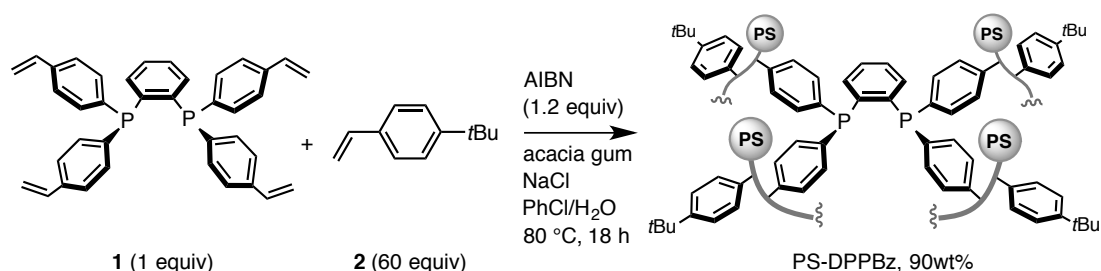


In a 300-mL round-bottom flask equipped with a magnetic stirring bar, a solution of *n*-BuLi in hexane (1.6 M, 5.5 mL, 8.8 mmol, 4.4 equiv) was slowly added to a solution of 4-bromostyrene (1.8 g, 9.7 mmol, 4.8 equiv) in THF (40 mL) at $-78\text{ }^{\circ}\text{C}$. After the mixture was stirred for 2 h at $-78\text{ }^{\circ}\text{C}$, a solution of 1,2-bis(dichlorophosphino)ethane (0.5 g, 2.2 mmol, 1 equiv) in THF (4 mL) was added over 5 min at $-78\text{ }^{\circ}\text{C}$. The mixture

was warmed to room temperature and stirred for 4 h. After quenching with aq. NH_4Cl , the mixture was extracted with CH_2Cl_2 . The organic layer was washed with water, dried over MgSO_4 , filtered and concentrated. The residue was purified by silica gel chromatography (97:3 hexane/EtOAc) to give **3** as white solids (0.48 g, 43% yield). White solids. M.p.: 115–116 °C ^1H NMR (400 MHz, CDCl_3): δ 2.06 (t, J = 4.0 Hz, 4H), 5.25 (d, J = 10.4 Hz, 4H), 5.75 (d, J = 17.2 Hz, 4H), 6.67 (dd, J = 17.2, 10.4 Hz, 4H), 7.22–7.29 (m, 8H), 7.30–7.40 (m, 8H). ^{13}C NMR (100.5 MHz, CDCl_3): δ 114.59 (s, 4C), 126.25 (t, $J_{\text{C-P}}$ = 2.9 Hz, 8C), 132.88 (t, $J_{\text{C-P}}$ = 9.6 Hz, 8C), 136.32 (s, 4C), 137.53 (t, $J_{\text{C-P}}$ = 7.6 Hz, 4C), 137.89 (s, 4C). ^{31}P NMR (161.8 MHz, CDCl_3): δ –13.0. IR (ATR) 691, 828, 905, 986, 1391, 1495, 1627 cm^{-1} . HRMS-ESI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{34}\text{H}_{32}\text{P}_2$, 503.20520; found, 503.20540.

3. Preparation of PS-Supported Ligands

PS-DPPBz

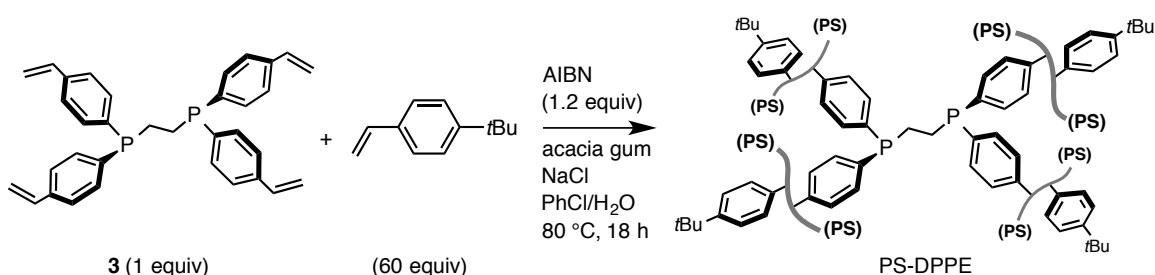


A solution of acacia gum (2.4 g) and NaCl (3.0 g) in water (60 mL) was placed in a 200-mL round-bottom flask equipped with a magnetic stirring bar, and was deoxygenated by purging with Ar. On the other hand, a solution of 4-(*tert*-butyl)styrene (2.4 g, >90% purity, 15 mmol), **4** (0.14 g, 0.25 mmol) and AIBN (0.049 g, 0.3 mmol) in chlorobenzene (3 mL) was degassed by three freeze-pump-thaw cycles, and was injected into the rapidly stirred aqueous solution. The mixture was stirred at 80 °C for 18 h. After it was cooled to room temperature, the mixture was filtered through a glass adaptor equipped with a cotton plug, washed successively with H_2O , MeOH, THF and toluene, and dried in vacuo at 80 °C for 12 h to give the polymer PS-DPPBz as white beads (2.3 g, 90 wt%). Obtained beads were passed through a series of sieves, and the beads with 250–710 μm size in diameter were used for a catalytic reaction. Combustion elemental analysis on P showed that the loading of the DPPBz moiety to PS resins was estimated to be 0.12 mmol/g, which was comparable to the theoretical value (0.10

mmol/g) on the assumption that all vinyl substrates were completely polymerized. The theoretical value of the DPPBz loading (0.10 mmol/g) will be used for metal complexation, regardless of this apparent underestimation.

^{31}P CP/MAS NMR (121.5 MHz): δ -17. **^{13}C CP/MAS NMR** (75.5 MHz): δ 34 ($-\text{C}(\text{CH}_3)_3$), 36 ($-\text{C}(\text{CH}_3)_3$), 37–59 ($-\text{CHArCH}_2-$), 120–139 (*Ar*), 145 (*Ar*), 150 (*Ar*). **Elemental Anal.** Found: C 89.15; H 9.87; P 0.72. (average for 2 runs).

PS-DPPE



A solution of acacia gum (2.4 g) and NaCl (3.0 g) in water (60 mL) was placed in a 200-mL round-bottom flask equipped with a magnetic stirring bar, and was deoxygenated by purging with Ar. On the other hand, a solution of 4-(*tert*-butyl)styrene (2.4 g, 15 mmol), **3** (0.12 g, 0.25 mmol) and AIBN (0.049 g, 0.30 mmol) in chlorobenzene (3 mL) was degassed by three freeze-pump-thaw cycles, and was injected into the rapidly stirred aqueous solution. The mixture was stirred at 80 °C for 18 h. After cooling to room temperature, the mixture was filtered through a glass adaptor equipped with a cotton plug, washed successively with H₂O, MeOH, THF and toluene, and dried in vacuo at 100 °C for 12 h to give the polymer PS-DPPE as white beads (2.1 g, 84 wt%). Obtained beads are passed through a series of sieves, and the beads with 250–710 μm size in diameter were used for the catalytic reaction. Combustion elemental analysis on P showed that the loading of the DPPE moiety to PS resins was estimated to be 0.13 mmol/g, which was comparable to the theoretical value (0.10 mmol/g) on the assumption that all vinyl substrates were completely polymerized. The theoretical value of the DPPE loading (0.10 mmol/g) will be used for metal complexation, regardless of this apparent underestimation.

^{31}P CP/MAS NMR (121.5 MHz): δ -15. **^{13}C CP/MAS NMR** (75.5 MHz): δ 33 ($-\text{C}(\text{CH}_3)_3$), 35 ($-\text{C}(\text{CH}_3)_3$), 37–60 ($-\text{CHArCH}_2-$), 127 (*Ar*), 145 (*Ar*), 150 (*Ar*). **Elemental Anal.** Found: C 88.90; H 9.79; P 0.82. (average for 2 runs).

4. Solis-Sate NMR Spectra of the PS-Supported Ligands

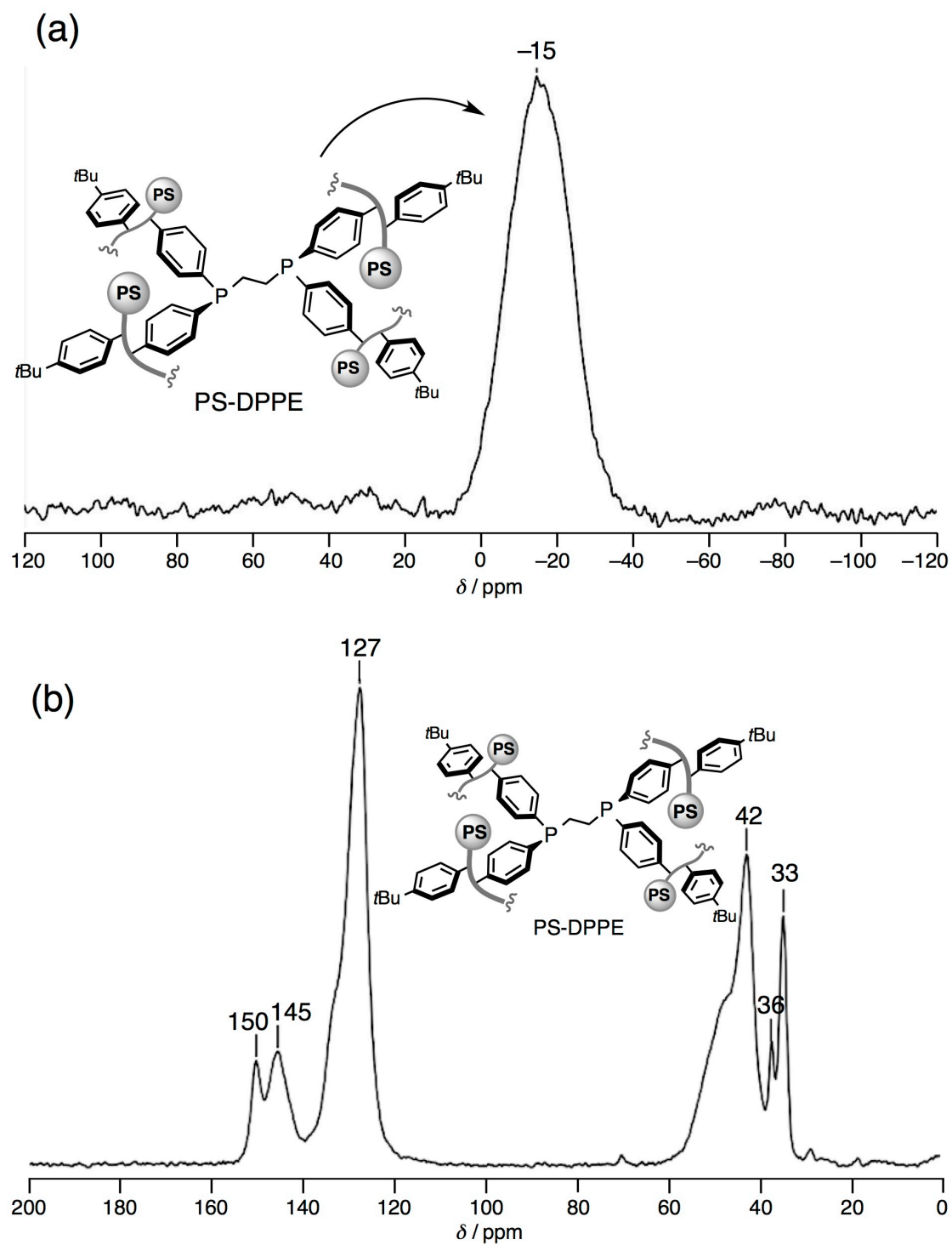


Figure 6. (a) ^{31}P CP/MAS and (b) ^{13}C CP/MAS NMR spectra of PS-DPPE.

5. Swelling Test of PS-DPPBz

A swelling test of PS-DPPBz was performed according to the literature.⁷ A graduated 1-mL syringe equipped with a filter paper at the exit was charged with 100 mg of the PS resin (original volume; 2.0 mL/g), and an appropriate solvent (1 mL) was added to the vessel. After the mixture was let stand for 15 min for equilibration, the extra solvent was removed from the syringe by using the plunger. The volume of the swollen resin was recorded (Table 1)

Table 1. Swelling property of PS-DPPBz in various solvents (volume in mL/g).

solvent	swelling volume (mL/g)
toluene	5.8
THF	5.8
CPME	6.0
1,4-dioxane	3.0
EtOAc	4.9
acetone	3.4
hexane	3.6
dimethylformamide	2.2
methanol	2.2
none	2.0

6. Reactions of [Rh(cod)₂]BF₄ and PS-DPPBz

PS-DPPBz (200 mg, 0.02 mmol) and [Rh(cod)₂]BF₄ (0.02 mmol, mg for Rh/P 1:1; 0.01 mmol, mg for Rh/P 1:2) were placed in a 5-mL glass tube containing a magnetic stirring bar. CH₂Cl₂ (2 mL) was added and stirred at room temperature for 2 h. The mixture was filtered through a glass adaptor equipped with a cotton plug, washed successively with CH₂Cl₂ and Et₂O, and dried in vacuo at room temperature 2 h. The mixture was analyzed with ³¹P CP/MAS NMR spectroscopy.

³¹P CP/MAS NMR (121.5 MHz): δ for Rh/P 1:1; 53. for Rh/P 1:2; 53, -17

7. Reactions of [Rh(cod)₂]BF₄ and DPPBz

DPPBz (0.02 mmol) and [Rh(cod)₂]BF₄ (0.02 mmol for Rh/DPPBz 1:1; 0.01 mmol for Rh/P 1:2) were placed in a 5-mL glass tube containing a magnetic stirring bar. CDCl₃ (1

mL) was added and stirred at room temperature for 10 min. The mixture was analyzed with ^{31}P NMR spectroscopy.

^{31}P NMR (161.8 MHz, CDCl_3): δ for Rh/DPPBz 1:1, 58.0 (d, $J_{\text{P-Rh}} = 147$ Hz), 62.8 (d, $J_{\text{P-Rh}} = 134$ Hz). For Rh/P 1:2, 62.8 (d, $J_{\text{P-Rh}} = 134$ Hz)

8. Preparations of $[\text{Rh}(\text{cod})(\text{DPPBz})]\text{BF}_4$ and $[\text{Rh}(\text{DPPBz})_2]\text{BF}_4$

$[\text{Rh}(\text{cod})(\text{DPPBz})]\text{BF}_4$

The mixture of DPPBz (22 mg, 0.049 mmol), $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20 mg, 0.049 mmol) and CH_2Cl_2 (2 mL) was stirred at room temperature for 1 h. The volatiles were evaporated. The residue was recrystallized from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ to give $[\text{Rh}(\text{cod})(\text{DPPBz})]\text{BF}_4$ as a orange solid (14 mg, 41% yield).

M.p.: 175 °C (decomp.). **^1H NMR** (400 MHz, CDCl_3): δ 2.30–2.50 (m, 8H), 5.08 (br-s, 4H), 7.47–7.58 (m, 20H), 7.58–7.61 (m, 4H). **^{13}C NMR** (100.5 MHz, CDCl_3): δ 29.95 (4C), 103.15 (4C), 129.48–129.80 (m, 8C), 129.95–130.80 (m, 4C), 131.82 (s, 4C), 132.50–132.95 (m, 8C), 133.13 (s, 4C), 141.40–142.45 (m, 2C). **^{31}P NMR** (161.8 MHz, CDCl_3): δ 56.0 (d, $J_{\text{P-Rh}} = 152$ Hz). **IR** (ATR) 670, 696, 725, 914, 998, 1024, 1052, 1095, 1433 cm^{-1} . **HRMS-ESI** (m/z) Calcd for $[\text{M-BF}_4]^+ \text{C}_{38}\text{H}_{36}\text{P}_2\text{Rh}$, 657.13473; found 657.13495.

$[\text{Rh}(\text{DPPBz})_2]\text{BF}_4$

The mixture of DPPBz (43 mg, 0.098 mmol), $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (20 mg, 0.049 mmol) and CH_2Cl_2 (2 mL) was stirred at room temperature for 2 h. The volatiles were evaporated. The residue was recrystallized from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ to give $[\text{Rh}(\text{DPPBz})_2]\text{BF}_4$ as a yellow solid (21 mg, 39% yield)

M.p.: >200 °C. **^1H NMR** (400 MHz, CDCl_3): δ 6.80–6.90 (m, 16H), 7.07–7.12 (m, 16H), 7.37–7.42 (m, 16H). **^{13}C NMR** (100.5 MHz, CDCl_3): δ 128.68 (s, 16C), 130.77 (s, 8C), 131.45–132.05 (m, 16C), 132.93 (s, 16C), 142.70–144.10 (m, 4C). **^{31}P NMR** (161.8 MHz, CDCl_3): δ 62.9 (d, $J_{\text{P-Rh}} = 134$ Hz). **IR** (ATR) 669, 692, 728, 740, 1024, 1048, 1093, 1433 cm^{-1} . **HRMS-ESI** (m/z) Calcd for $[\text{M-BF}_4]^+ \text{C}_{60}\text{H}_{38}\text{P}_4\text{Rh}$, 995.17615; found 995.17544.

9. Reactions of $\text{Pd}(\text{cod})\text{Cl}_2$ and PS-Bisphosphines

PS-bisphosphine beads (200mg, 0.02 mmol) and $[\text{Pd}(\text{cod})\text{Cl}_2]$ (11mg, 0.04 mmol) were

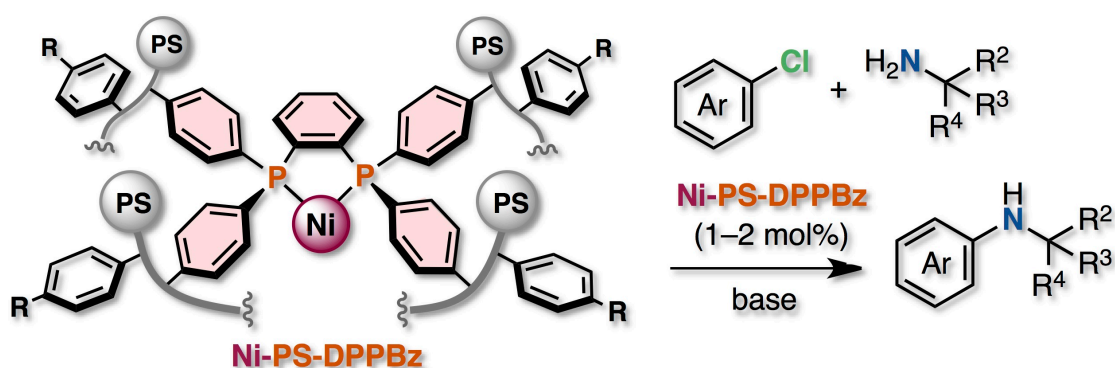
placed in a 5-mL glass tube containing a magnetic stirring bar. THF (4 mL) was added and stirred at room temperature for 12 h. The mixture was filtered through a glass adaptor equipped with a cotton plug, washed successively with CH₂Cl₂ and Et₂O, and dried in vacuo at room temperature 2 h. The mixture was analyzed with ³¹P CP/MAS NMR spectroscopy. ³¹P CP/MAS NMR (121.5 MHz): δ for PS-DPPBz; 60 [PdCl₂(PS-DPPBz)], for PS-DPPE; 33, 63

Reference and Notes

- (1) Example of polymer supported bisphosphine ligands, see; (a) Lu, Y.; Plocher, E.; Hu, Q. S. *Adv. Synth. Catal.* **2006**, *348*, 841–845. (b) Wang, P. W.; Fox, M. A. *J. Org. Chem.* **1994**, *59*, 5358–5364. (c) Champness, N. R.; Levason, W.; Oldroyd, R. D. *J. Organomet. Chem.* **1994**, *465*, 275–281. (d) Stille, J. K.; Su, H.; Hill, D. H.; Schneider, P.; Tanaka, M.; Morrison, D. L.; Hegedus, L. S. *Organometallics*, **1991**, *10*, 1993–2000. (e) Benvenuti, F.; Carlini, C.; Marchionna, M.; Parlini, R.; RaspolliGalletti, A. M.; Sbrana, G. *J. Organomet. Polym. Chem.* **1997**, *7*, 183.
- (2) For selected examples of polymer-crosslinked bisphosphines, see; (a) Sun, Q.; Dai, Z.; Liu, X.; Sheng, N.; Deng, F.; Meng, X.; Xiao, F. S. *J. Am. Chem. Soc.* **2015**, *137*, 5204–5209. (a) Brunkan, N. M.; Gagné, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 6217–6225. (b) Voshell, S. M.; Gagné, M. R. *Organometallics* **2005**, *24*, 6338–6350.
- (3) Metal-organic frameworks with a DPPBz scaffold: Bohnsack, A. M.; Ibarra, I. A.; Bakhmutov, V. I.; Lynch, V. M. *J. Am. Chem. Soc.* **2013**, *135*, 16038–16041.
- (4) Iwai, T.; Harada, T.; Hara, K.; Sawamura, M. *Angew. Chem. Int. Ed.* **2013**, *52*, 12322–12326.
- (5) Combustion elemental analysis on P showed that the loading of the DPPBz moiety to PS resins was estimated to be 0.12 mmol/g. In this paper, we used the loading value of 0.10 mmol/g based on the monomer ratio for metal complexations and catalytic applications.
- (6) Xiao and co-worker used same phosphine monomer as templates for porous organic ligand, see ref. 2a
- (7) R. Santini, M. C. Griffith, M. Qi, *Tetrahedron Lett.* **1998**, *39*, 8951.

Chapter 3

Ni-(PS-DPPBz)-Catalyzed Amination of Chloroarenes with Primary Alkylamines



ABSTRACT: Use of a newly developed bisphosphine-branched polystyrene (PS-DPPBz) enabled highly efficient Ni-catalyzed amination of chloroarenes with primary alkylamines. Owing to polymer effects to bisphosphine-bound active Ni centers, the Ni-PS-DPPBz system exhibited high catalytic efficiency in a relatively high temperature range, allowing challenging amination reactions with sterically congested and/or electronically deactivated substrates.

Introduction

Transition-metal-catalyzed amination of haloarenes is a powerful method for the preparation of arylamines.¹ While Pd is the most common metal for this catalysis, using Ni as a more earthly abundant alternative to Pd is an attractive strategy for pursuing environmentally benign organic synthesis.² Recently, Hartwig and co-workers reported highly efficient Ni-catalyzed protocols for amination of haloarenes³: (BINAP)Ni(η^2 -NC-Ph) was introduced as a catalyst precursor that enabled ever-challenging reactions between unactivated chloroarenes and primary aliphatic amines (Scheme 1a).⁴⁻⁶ Mechanistic studies by Hartwig and co-workers indicated the importance of controlled Ni monochelation by the BINAP bisphosphine ligand.

This chapter describes that a newly developed bisphosphine-branched polystyrene was favorable for controlled Ni monochelation and produced a high-performing heterogeneous amination catalyst in combination with Ni(cod)₂. The new heterogeneous catalyst dramatically expanded the substrate scope of Ni-catalyzed amination of chloroarenes with primary alkylamines, enabling the use of electronically and/or sterically deactivated chloroarenes and primary aliphatic amines involving tertiary alkyl groups as *N*-substituents.

Results and Discussion

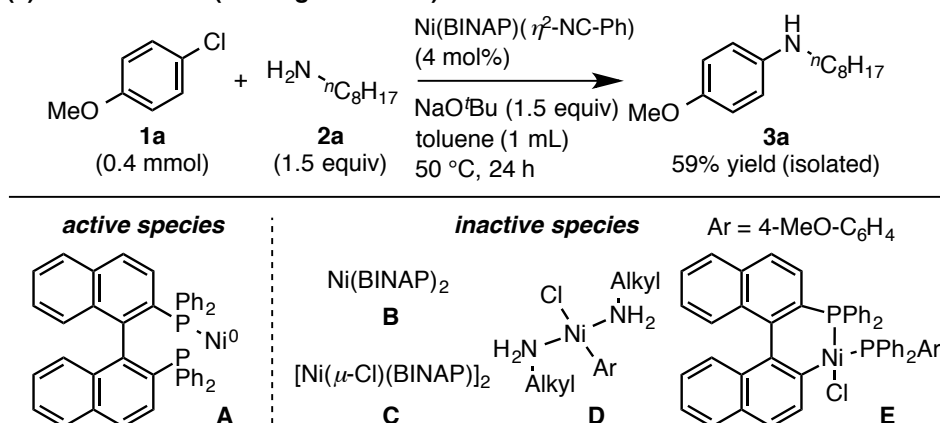
Hartwig and co-workers indicated that a bisphosphine-monochelated Ni(0) complex (BINAP)Ni(0) formed by reversible dissociation of PhCN from (BINAP)Ni(η^2 -NC-Ph) is a catalytically active species that reacts with an aryl chloride.³ In addition, they identified four catalytically inactive species, (BINAP)₂Ni(0) (**A**), [(BINAP)Ni(η^2 -Cl)]₂ (**B**), NiCl₂(amine)₂ (**C**), and a nickelacycle complex (**D**), which limited the catalytic activity and scope of the reaction. Specifically, the reaction of 4-chloroanisole (**1a**), which was deactivated by an electron-donating *p*-MeO group, with *n*-octylamine (**2a**) required relatively high catalyst loading (4 mol%) to obtain an acceptable yield of coupling product **3a** (Scheme 1a).

The author sought that the formation of the inactive species **A** and **B**, both of which have two bisphosphine ligands, could be inhibited by immobilizing the bisphosphine units on a solid support with effective spatial isolation (Scheme 1b). As one of the ideal

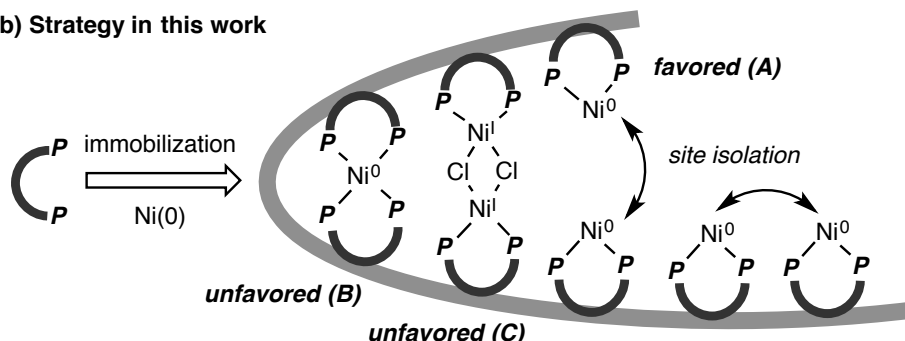
ways to achieve this, we envisaged to prepare bisphosphine-branched polystyrenes based on the knowledge of usefulness of the triphenylphosphine-branched polystyrenes (PS-TPP, its structure shown in Table 1) as heterogeneous monophosphine ligands to achieve controlled mono-P-ligation to metals (P/M 1:1; M = Pd, Rh, Ir) in some challenging metal catalysis.⁷

Scheme 1. Ni-catalyzed amination of chloroarenes with primary alkylamines.

(a) Previous work (Hartwig et al. 2014)

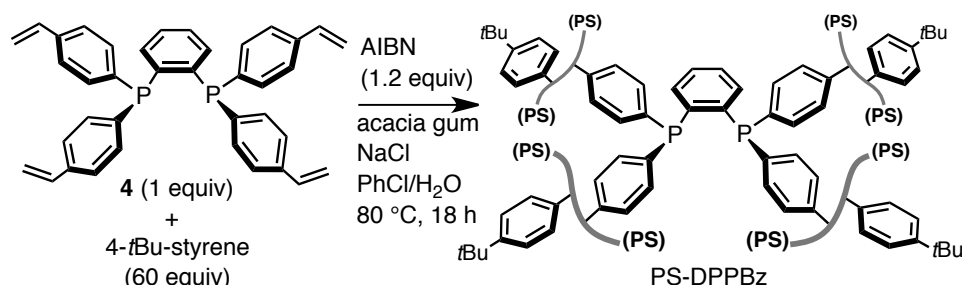


(b) Strategy in this work



In fact, the author synthesized a bisphosphine-branched polystyrene (PS-DPPBz), having a 1,2-bis(diphenylphosphino)benzene (DPPBz) core, through radical emulsion polymerization with tetravinylated DPPBz (**4**)⁸⁻¹⁰ and 4-*t*-butylstyrene (**4**: 4-*t*-butylstyrene 1:60) (Scheme 2). The rigid DPPBz core was adopted as a bisphosphine unit to gain better metal chelation ability in a polymer matrix.¹¹ This nature may also be beneficial for suppressing the ligand substitution between bisphosphines and amines to form **D**. In addition, the rigid nature of the bisphosphine backbone may suppress the ligand degradation due to P-C bond cleavage as in the formation of **E**.

Scheme 2. Preparation of PS-DPPBz



To investigate a coordination property of PS-DPPBz toward a Ni(0) complex, the reaction of PS-DPPBz with excess Ni(cod)₂ (2:1 Ni/PS-DPPBz) was conducted in benzene at 60 °C for 10 min. After filtration, washing and drying, a solid-state ³¹P CP/MAS NMR analysis of the obtained red beads showed a broad signal at δ 39 (Figure 1a.), indicating that all bisphosphine participated in coordination to the Ni complex. Even with excess bisphosphines toward the Ni complex (1:2 Ni/PS-DPPBz), the signal at δ 39 remained intact (Figure 1b.). In contrast, the use of the soluble ligand DPPBz in C₆D₆ (1:1 Ni/DPPBz) gave two ³¹P signals at δ 56 and 48 (Figure 2a.), indicating formations of the 1:1 Ni/DPPBz complex Ni(cod)(DPPBz) and the 1:2 Ni/DPPBz complex Ni(DPPBz)₂, respectively (Figure 2b.). Although the signal at δ 39 in the heterogeneous Ni(cod)₂/PS-DPPBz system could not be assigned at present, the author believes that PS-DPPBz is favorable for controlled Ni monochelation because of effective site isolation by the polymer effects^{12,13}.

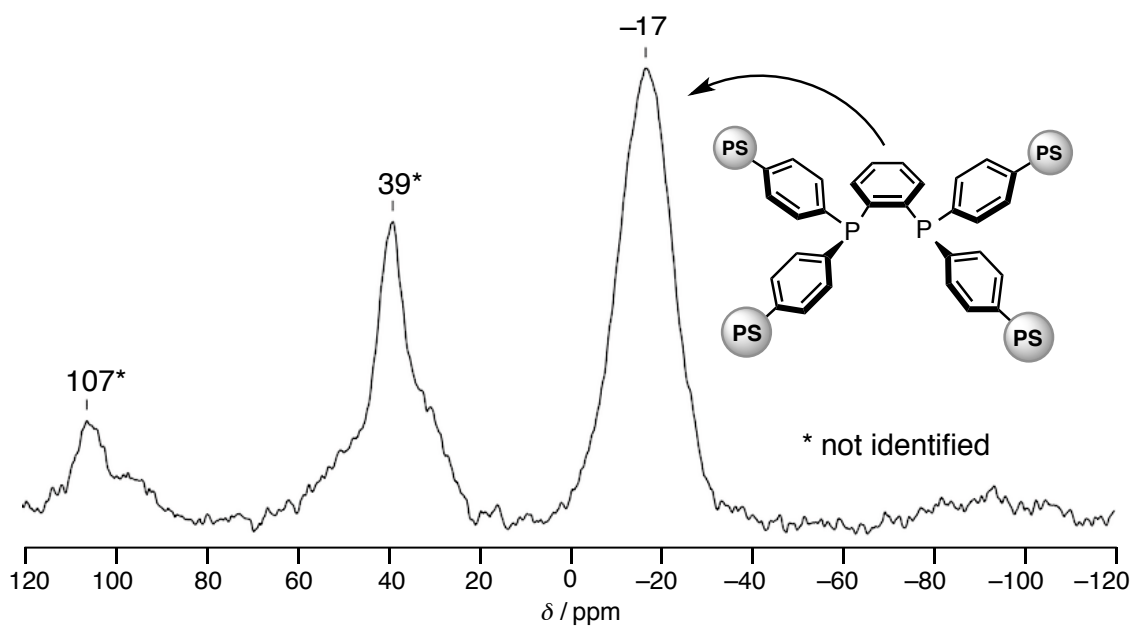
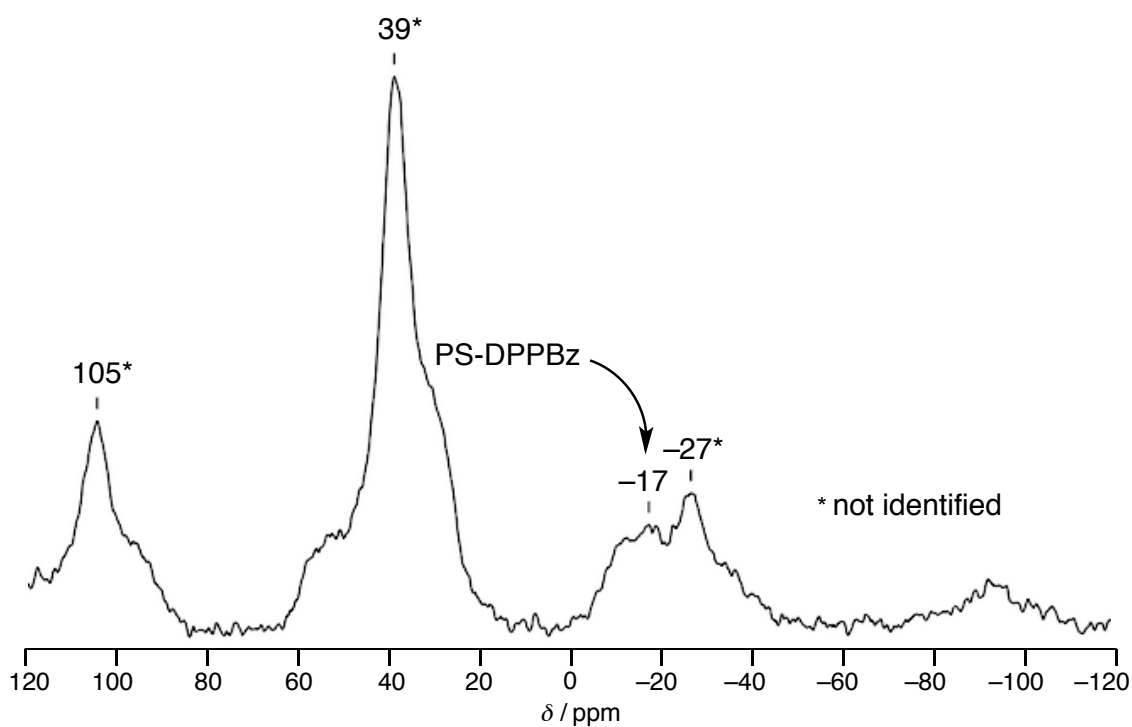


Figure 1. ^{31}P CP/MAS spectrum obtained from $\text{Ni}(\text{cod})_2$ and PS-DPPBz [(a) 2:1 Ni/PS-DPPBz, (b) 1:2 Ni/PS-DPPBz]

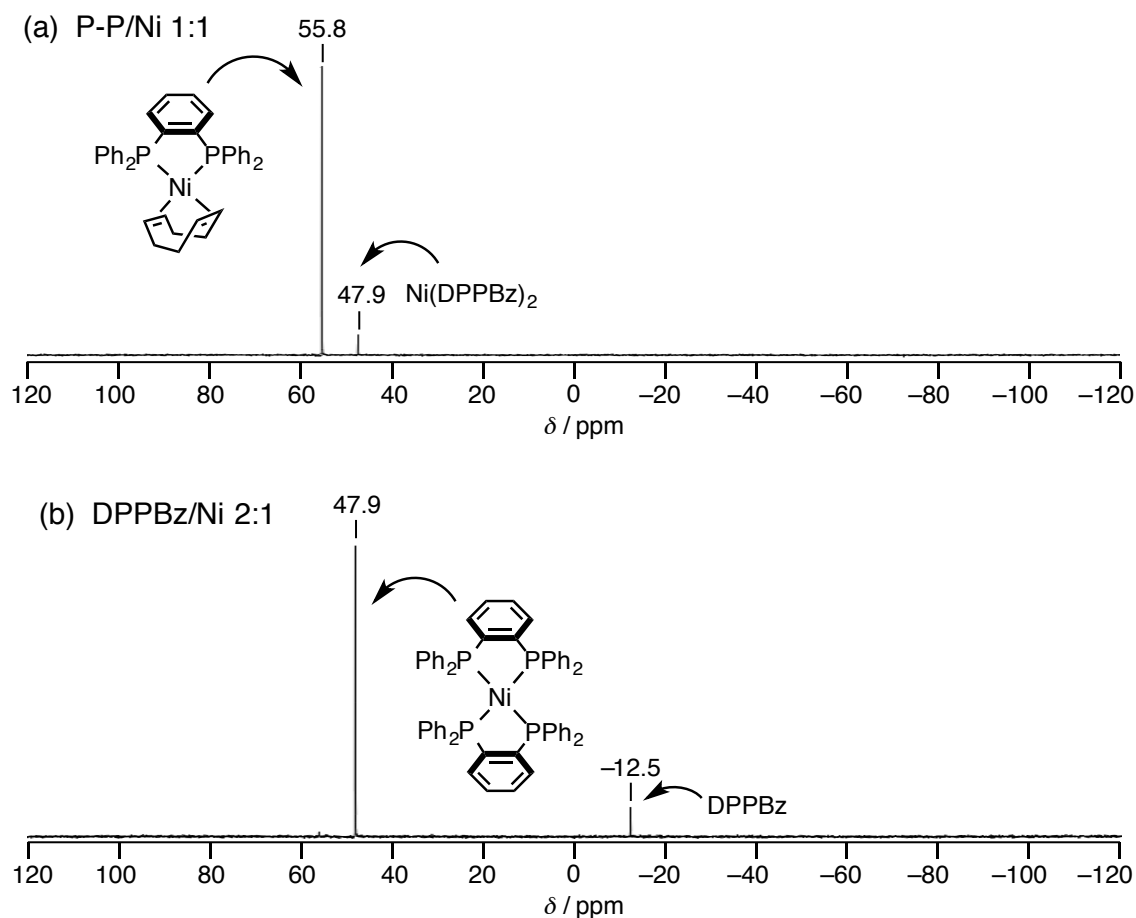


Figure 2. ^{31}P NMR spectrum in C_6D_6 obtained from $\text{Ni}(\text{cod})_2$ and DPPBz [(a) 1:1 Ni/ DPPBz, (b) 1:2 Ni/ DPPBz]

These results promoted the author to investigate the ligand performance of PS-DPPBz in the Ni-catalyzed amination of chloroarenes with primary alkylamines. Initially, various homogeneous and heterogeneous ligands were evaluated in the C–N coupling between 4-chloroanisole (**1a**) and *n*-octylamine (**2a**) with 1 mol% of the catalyst loading in the presence of NaOtBu (1.5 equiv) as base. The results are summarized in Table 1.

The Hartwig's precatalyst $(\text{BINAP})\text{Ni}(\eta^2\text{-NC-Ph})$ promoted the amination at 50 °C as mentioned in Scheme 1, but the yield of the coupling product **3a** was decreased to 22% due to a decreasing catalytic loading (Table 1, entry 1). Elevated temperature to 80 °C was not so effective. Use of BINAP as a ligand in combination with $\text{Ni}(\text{cod})_2$ as a metal source was comparable to $(\text{BINAP})\text{Ni}(\eta^2\text{-NC-Ph})$ (entry 2). The homogeneous DPPBz induced little activity even at 80 °C (entry 3). During further screening of homogeneous ligands based on related Ni catalysis using ammonia as an amine source,

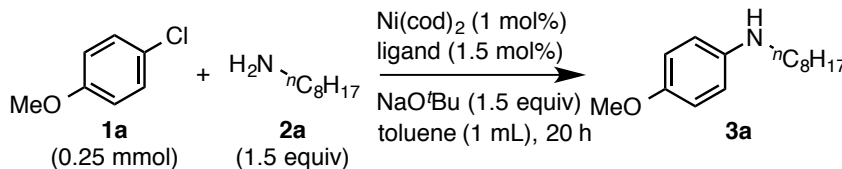
the author found that a cyclohexyl-substituted Josiphos-type ligand **5** effectively promoted the amination at 80 °C to give **3a** in 94% yield (entry 4).⁴ The advance of the PS-DPPBz over homogeneous systems is more significant in the reactions of sterically demanding substrates (*vide infra*).

Although an immobilized catalyst system Ni-PS-DPPBz, which was prepared in situ from Ni(cod)₂ and PS-DPPBz, showed low efficiency at 50 °C, the catalytic performance was significantly improved at 80 °C to afford **3a** quantitatively (Table 1, entry 5). These results indicated that PS-DPPBz could produce the efficient Ni catalyst with high thermal stability through formation of five-membered chelation. The catalytic loading of Ni-PS-DPPBz can be reduced to 0.1 mol% at 120 °C without significant loss of the yield (93% isolated yield, Scheme 3.).

When a catalytic amount of DPPBz (1.5 mol%) was added to the Ni-PS-DPPBz system at 80 °C, the catalytic activity disappeared completely (Table 1, entry 6) probably due to formation of inactive 1:2 Ni(0)-bisphosphine species and/or Ni leaching. The selective mono-ligating feature of PS-DPPBz toward the Ni center is owing to the polymer effects for effective site isolation.

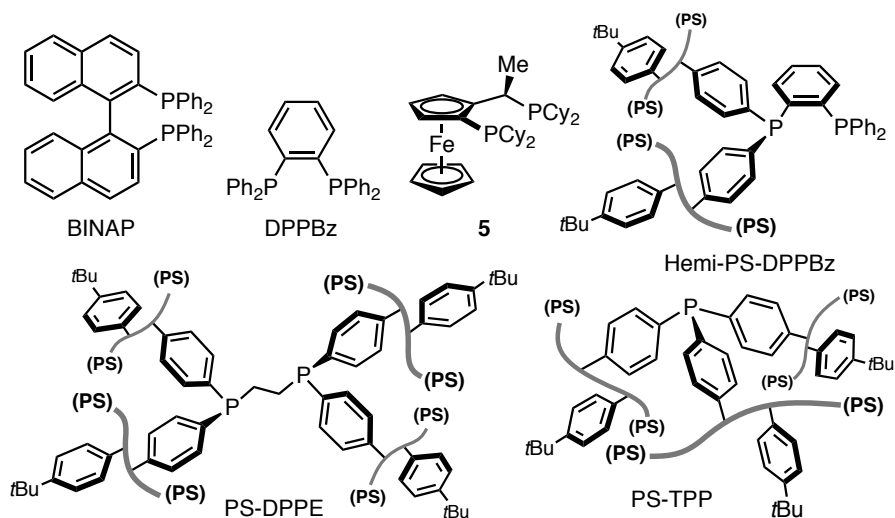
A twofold cross-linking bisphosphine Hemi-PS-DPPBz induced less efficient amination (Table 1, entry 7). A fourfold polystyrene-cross-linking DPPE-based ligand PS-DPPE did not provide **3a** at all probably due to inhibition of *s-trans* to *s-cis* conformational change of the flexible DPPE backbone in the polymer matrix (entry 8). The PPh₃-branched polystyrene PS-TPP was totally ineffective (entry 9). These results suggested that fourfold-crosslinking DPPBz core is crucial for the high catalytic activity.

Table 1. Ligand effects in Ni-catalyzed amination of **1a** with **2a**.^a

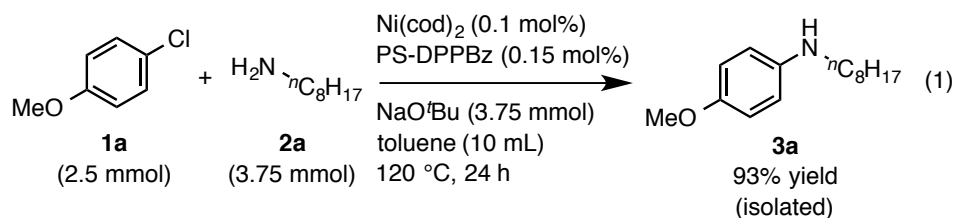
			
entry	ligand	yield (%) ^b [at 50 °C]	yield (%) ^b [at 80 °C]
1 ^c	—	22	31

2	BINAP	18	30
3	DPPBz	0	6
4	5	61	94
5	PS-DPPBz	23	>99 (89)
6 ^d	PS-DPPBz + DPPBz	—	0
7	Hemi-PS-DPPBz	—	12
8	PS-DPPE	—	0
9 ^e	PS-TPP	—	0

^a Conditions: **1a** (0.25 mmol), **2a** (0.375 mmol), Ni(cod)₂ (1 mol%), ligand (1.5 mol%), NaOtBu (0.375 mmol), toluene (1 mL), 50 or 80 °C, 20 h. ^b Yields were determined by ¹H NMR analysis of the crude product. Isolated yields were shown in parentheses. ^c The use of Ni(BINAP)(*h*²-NC-Ph) instead of Ni(cod)₂. ^d PS-DPPBz (1.5 mol%), DPPBz (1.5 mol%). ^e PS-TPP (3 mol%).



Scheme 3. Reaction with lower catalyst loading



The utility of Ni-PS-DPPBz catalyst system was clearly demonstrated in the amination of sterically demanding chloroarenes. As shown in Table 2, di-*ortho*-substituted chloroarenes such as 2,6-dimethylchlorobenzene and 2,6-diisopropylchlorobenzene successfully reacted with **2a** at 100–120 °C in the presence of 1 mol% of Ni-PS-DPPBz, giving **3b** and **3c** in high yields. Sterically, as well as electronically deactivated chloroarene 2,4,6-trimethoxychlorobenzene was also applicable to the amination. In contrast, use of BINAP and **5** as a ligand under otherwise same conditions was much less efficient (0~20% yields).

The broad scope of chloroarenes with the Ni-PS-DPPBz system is also demonstrated in Table 2. Electron-rich chloroarenes (**3e–3g**), electron-neutral (**3h**), electron-deficient (**3i** and **3j**) and π -extended (**3k**) chloroarenes successfully underwent the amination with **2a** at 80–100 °C, to give desired products in good to high yields (69–97%). 3-Pyridyl (**3l**) chlorides served as a suitable substrate. Amination of mono-*ortho*-substituted chloroarenes such as 2-chlorotoluene and 2-chloroanisole smoothly proceeded at 80 °C to give *o*-substituted anilines (**3m** and **3n**) in high yields.

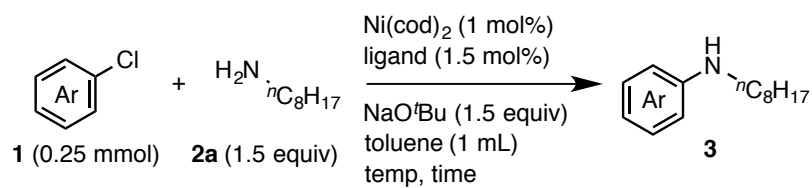
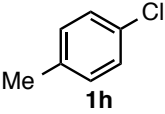
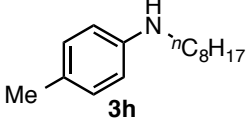
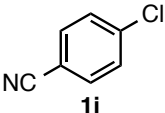
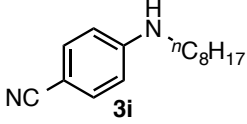
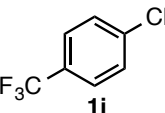
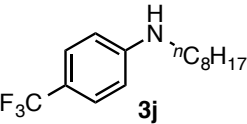
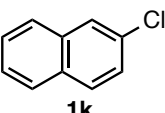
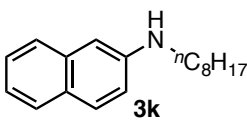
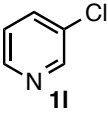
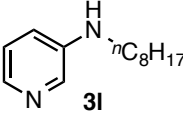
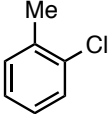
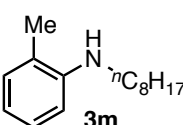
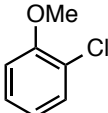
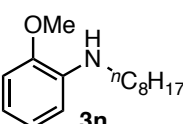


Table 2. Ni-catalyzed amination of chloroarenes with **2a**.^{a, b}

entry	Aryl chloride 1	ligand 5	Temp. (°C)	Time (h)	Product 3	Yield ^b (%)
1		PS-DPPBz BINAP 5	100	20	 3b	97 0 20
2		PS-DPPBz BINAP 5	120	24	 3c	92 0 0
3		PS-DPPBz BINAP 5	120	24	 3d	80 0 0
4		PS-DPPBz	80	20	 3e	69
5		PS-DPPBz	100	20	 3f	92
6		PS-DPPBz	100	20	 3g	88

7		PS-DPPBz	80	20		80
8		PS-DPPBz	80	20		90
9 ^c		PS-DPPBz	80	20		93
10		PS-DPPBz	80	20		96
11		PS-DPPBz	80	20		94
12		PS-DPPBz	80	20		97
13		PS-DPPBz	80	20		93

^a Conditions: **1** (0.25 mmol), **2a** (0.375 mmol), Ni(cod)₂ (1 mol%), ligand (1.5 mol%), NaOtBu (0.375 mmol), toluene (1 mL), 80–120 °C, 20 h. ^b Isolated yields. ^c The use of LiOtBu instead of NaOtBu.

The scope of primary alkylamines with the Ni-PS-DPPBz system was also expanded (Table 3). Isoamyl (**3o**) and 2-phenethyl (**3p**), 4-methoxybenzyl (**3q**) amines smoothly reacted under the standard conditions (1 mol% Ni, 80 °C, 20 h) to give the corresponding secondary amines in high yields. The reactions of amines containing cyclic and acyclic secondary alkyl groups proceeded in high yields (**3r**). Although primary amines containing tertiary alkyl groups at the position *a* to the N atom afforded low yields of the desired products under the present optimal conditions (data not shown), use of LiOtBu instead of NaOtBu as base significantly improved the reaction efficiency. For example, 1-adamatylamine (**3s** and **3t**), *t*-amylamine (**3u** and **3v**) and cumylamine

(**3w**) successfully participated in this transformation at 120 °C with reasonable catalyst loading (1–2 mol% Ni), giving hindered secondary amines in good-to-high yields. This is the first example of the use of α -trisubstituted primary amines for the C–N coupling with Ni catalysts.^{14, 15}

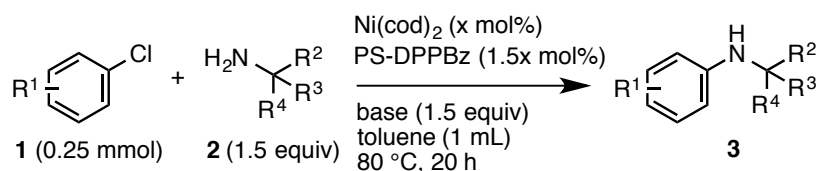


Table 3. Substrate scope of primary alkylamines^a.

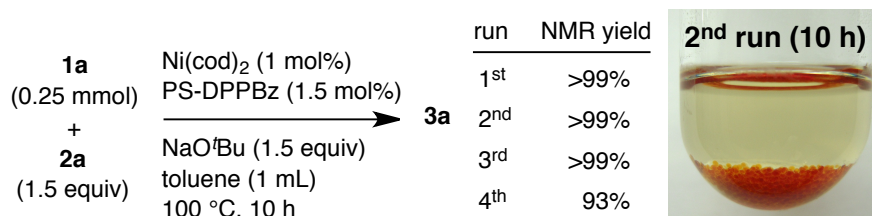
entry	ArCl 1	Amine 2	Ni cat. (mol%)	base	Product 3	Yield ^b (%)
1	1a		1	NaO ^t Bu		77
2	1a		1	NaO ^t Bu		94
3	1a		1	NaO ^t Bu		96
		Ar = <i>p</i> -OMe-C ₄ H ₄				
4	1a		1	NaO ^t Bu		94
5 ^c	1h		1	LiO ^t Bu		83
6 ^c	1a	2f	1	LiO ^t Bu		77



^a Condition: **1** (0.25 mmol), **2** (0.375 mmol), Ni(cod)₂ (1 mol%), PS-DPPBz (1.5 mol%), NaO^tBu (0.375 mmol), toluene (1 mL), 80 °C, 20 h. ^b Isolated yields. ^c at 120 °C. ^d toluene (0.5 mL).

The heterogeneous catalyst system Ni-PS-DPPBz showed good reusability for the C–N coupling reaction between **1a** and **2a**, as shown in Scheme 3 (1 mol% Ni, 100 °C, 10 h). The immobilized Ni catalyst could easily be separated and reused at three times without significant loss of the product yield (1st run, >99%; 2nd run, >99%; 3rd run, >99%; 4th run, 93%; determined by ¹H NMR analysis). However, the consecutive Ni leaching was observed (4.0~5.6% of the loaded Ni for each run, detected by ICP-AES). The Ni leaching may be due to the partial ligand substitution of the Ni center by amine substrates (**C** in Scheme 1).

Scheme 3. Reuse of Ni-PS-DPPBz system.



Conclusion

The author developed a highly efficient Ni catalyst with a bisphosphine-branched polystyrene PS-DPPBz for amination of chloroarenes with primary alkylamines. Owing to the polymer effects to bisphosphine-bound active Ni centers, the Ni-PS-DPPBz

system exhibited high catalytic efficiency in a relatively high temperature range, thus enabling it to be applicable to sterically and/or electronically challenging substrates, for which reported protocols were not applicable. The present work supports catalyst deactivation mechanisms reported previously, and thus immobilized bisphosphines such as PS-DPPBz would be useful for a mechanistic study.

Experimental Section

1. Instrumental and Chemicals

Solution NMR spectra were recorded on a JEOL ECX-II (400 MHz for ^1H NMR, 100.5 MHz for ^{13}C NMR, and 161.8 MHz for ^{31}P NMR) and on Varian Gemini 2000 spectrometer (300 MHz for ^1H NMR) unless otherwise noted. Chemical shift values are referenced to Me_4Si (^1H), the residual solvent (^{13}C), and H_3PO_4 (^{31}P). Magic angle spinning (MAS) NMR spectra were recorded on a Bruker MSL-300 spectrometer, operating at 75.5 MHz for ^{13}C NMR, and 121.5 MHz for ^{31}P NMR. EI-MS spectra were recorded on a JEOL JMS-Q1050GC. High-resolution mass spectra (Thermo Scientific Exactive or JEOL JMS-T100LC for ESI-MS) were recorded at the Instrumental Analysis Division, Equipment Management Center, Creative Research Institution, Hokkaido University. Elemental analyses were performed at Center for Organic Elemental Microanalysis, Graduate School of Pharmaceutical Science, Kyoto University. ICP-AES analyses (Shimadzu ICPE-9000) were performed at Hokkaido University Sousei Hall. A microwave digestion system (Milestone, ETHOS One) was used to prepare samples for ICP-AES analyses. GLC analyses were conducted on a Shimadzu GC-14B equipped with a flame ionization detector. Melting points were determined on a micro melting point apparatus using micro cover glass (Yanaco MP-500D). TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F₂₅₄. Silica gel (Kanto Chemical Co., Ltd., Silica gel 60 N, spherical, neutral) was used for column chromatography.

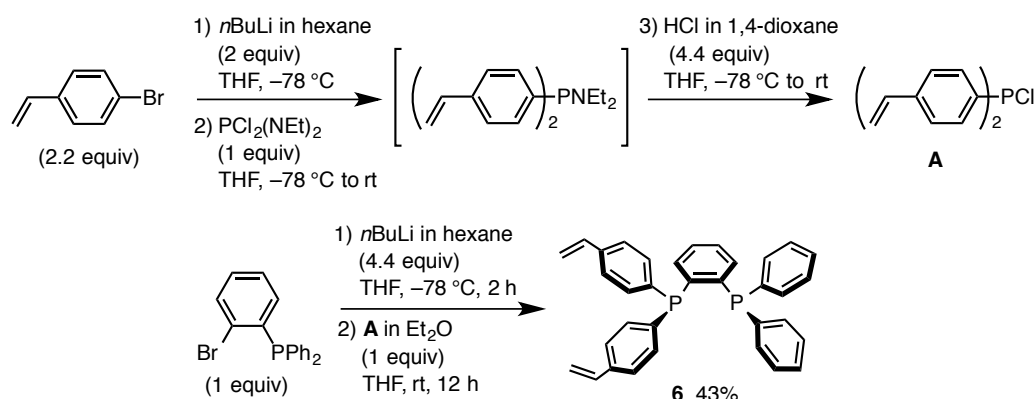
All reactions were carried out under nitrogen or argon atmosphere. Materials were obtained from commercial suppliers or prepared according to standard procedures unless otherwise noted. 1,2-Bis(dichlorophosphino)benzene was purchased from Wako Pure Chemical Industries, Ltd. Divinylbenzene (*m*- and *p*-mixture, contains ethylvinylbenzene and ethylbenzene, >50% GC purity, stabilized with TBC),

4-*t*-butylstyrene (>90% GC purity, stabilized with TBC) were purchased from TCI Co., Ltd., and were purified by passing through a alumina column before use (Alumina Activated 200, Nakarai Tesque, Inc.). 2,2'-Azo bis(isobutyronitrile) (AIBN) was purchased from Junsei Chemical Co. Ltd. Acacia gum was purchased from Nacalai Tesque, Inc. NaO*t*Bu and LiO*t*Bu were purchased from TCI Co., Ltd. and Aldrich Co., Ltd., respectively. Ni(cod)₂ was purchased from Kanto Chemical Co., Ltd., and was recrystallized from toluene/1,5-cyclooctadiene before use. PS-TPP was prepared according to the literature.⁷ All solvents for catalytic reactions were degassed via three freeze–pump–thaw cycles.

2. Preparation of Homogeneous Ligands

Phosphine monomer 4 was prepared according to the procedure shown in chapter 2.

(2-(Bis(4-vinylphenyl)phosphino)phenyl)diphenylphosphine (6)



In 100-mL of a round-bottom flask equipped with a magnetic stirring bar, a solution of *n*BuLi in hexane (1.6 M, 1.9 mL, 3.0 mmol, 1 equiv) was slowly added to a solution of (2-bromophenyl)diphenylphosphine (1.0 g, 2.9 mmol, 1 equiv) in THF (20 mL) at -78 °C, and the mixture was stirred for 2 h at this temperature. On the other hand, chlorobis(4-vinylphenyl)phosphine was prepared by a following procedure; in a 20-mL schlenk flask, dichloro(diethylamino)phosphine (0.5 g, 3 mmol, 1 equiv) was added to a solution of (4-vinylphenyl)lithium, which was prepared from 4-bromostyrene (1.2 g, 6.6 mmol, 2.2 equiv) and *n*BuLi (1.6 M in hexane, 3.8 mL, 6 mmol, 2 equiv) in THF (10 mL) at -78 °C, and the mixture was stirred for 1 h at -78 °C. After it was warmed to room temperature, the mixture was again cooled to -78 °C. After HCl in 1,4-dioxane (4 M, 3.3 mL, 13.2 mmol, 4.4 equiv) was added at -78 °C, the mixture was stirred for 1 h at -78 °C and then warm to room temperature. The volatile was removed, and the

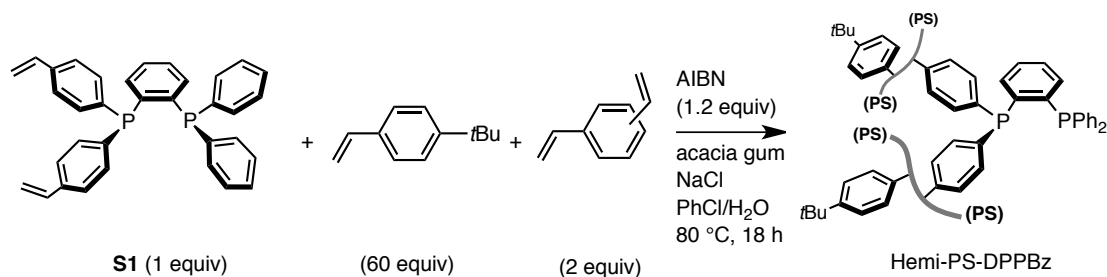
residue was suspended with Et₂O. The solution of chlorobis(4-vinylphenyl)phosphine (3 mmol based on dichloro(diethylamino)phosphine) was slowly transferred to the 100-mL round-bottom flask with the aryllithium reagent via cannula capped with a filter paper at –78 °C. The mixture was warmed to room temperature and stirred for 12 h. After quenching with aq. NH₄Cl, the mixture was extracted with CH₂Cl₂. The organic layer was washed with water, dried over MgSO₄, filtered and concentrated. The residue was purified by silica gel chromatography (97:3 hexane/EtOAc) to give **6** as white solids (0.65 g, 43% yield).

White solids. **M.p.**: 63–65 °C ¹H NMR (400 MHz, CDCl₃): δ 5.25 (d, *J* = 10.8 Hz, 2H), 5.74 (d, *J* = 16.8 Hz, 2H), 6.67 (dd, *J* = 10.8, 16.8 Hz, 2H), 7.02–7.10 (m, 2H), 7.10–7.19 (m, 8H), 7.19–7.30 (m, 10H). ¹³C NMR (100.5 MHz, CDCl₃): δ 116.02 (2C), 126.02 (2C), 126.06 (2C), 128.22 (4C), 129.02 (2C), 129.05 (2C), 133.50–134.50 (m, 10C), 136.36–136.48 (m, 4C), 136.79 (1C), 136.86 (1C), 137.49 (2C), 143.20–143.75 (2C). ³¹P NMR (161.8 MHz, CDCl₃): δ –14.1, –14.0. **IR** (ATR) 694, 742, 832, 909, 988, 1090, 1392, 1434, 1494 cm^{–1}. **HRMS-ESI** (*m/z*): [*M*]⁺ calcd for C₃₄H₂₈P₂, 498.16530; found, 498.16662.

3. Preparation of PS-Supported Ligands

PS-DPPBz and PS-DPPE were prepared according to the procedure shown in chapter 2.

Hemi-PS-DPPBz

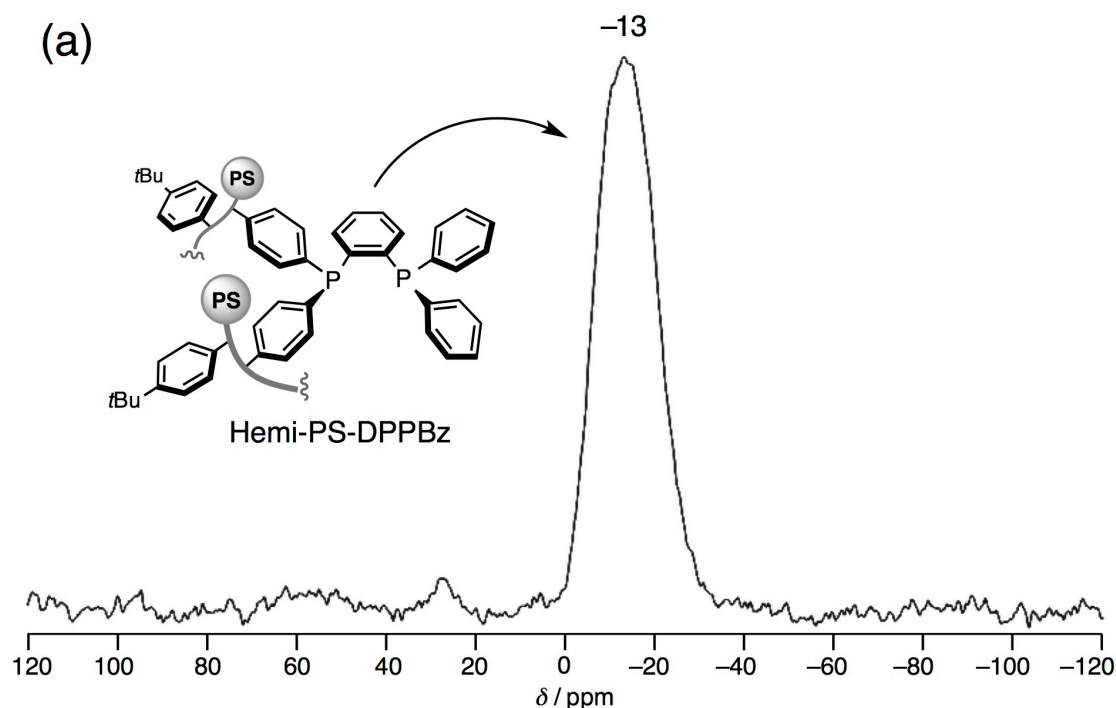


A solution of acacia gum (2.4 g) and NaCl (3.0 g) in water (60 mL) was placed in a 200-mL round-bottom flask equipped with a magnetic stirring bar, and was deoxygenated by purging with Ar. On the other hand, a solution of 4-(*tert*-butyl)styrene (2.4 g, >90% purity, 15 mmol), **6** (0.12 g, 0.25 mmol), divinylbenzene (0.065 g, >50% purity, 0.5 mmol) and AIBN (0.049 g, 0.3 mmol) in chlorobenzene (3 mL) was degassed by three freeze-pump-thaw cycles, and was injected into the rapidly stirred aqueous solution. The mixture was stirred at 80 °C for 18 h. After it was cooled to room

temperature, the mixture was filtered through a glass adaptor equipped with a cotton plug, washed successively with H₂O, MeOH, THF and toluene, and dried in vacuo at 100 °C for 12 h, to give the polymer hemi-PS-DPPBz as white beads (2.0 g, 76 wt%). Obtained beads are passed through a series of sieves, and the beads with 250–710 μ m size in diameter were used for catalytic reactions. Combustion elemental analysis on P showed that the loading of the DPPBz moiety to PS resins was estimated to be 0.16 mmol/g, which was comparable to the theoretical value (0.10 mmol/g) on the assumption that all vinyl substrates were completely polymerized. The theoretical value of the DPPBz loading (0.10 mmol/g) will be used for metal complexation and catalytic reactions, regardless of this apparent underestimation.

³¹P CP/MAS NMR (121.5 MHz): δ -15. **¹³C CP/MAS NMR** (75.5 MHz): δ 34 (–C(CH₃)₃), 36 (–C(CH₃)₃), 37–59 (–CHArCH₂–), 127 (*Ar*), 145 (*Ar*), 150 (*Ar*). **Elemental Anal.** Found: C 88.94; H 9.81; P 1.11. (average for 2 runs).

4. Solis-Sate NMR Spectra of the PS-Supported Ligands



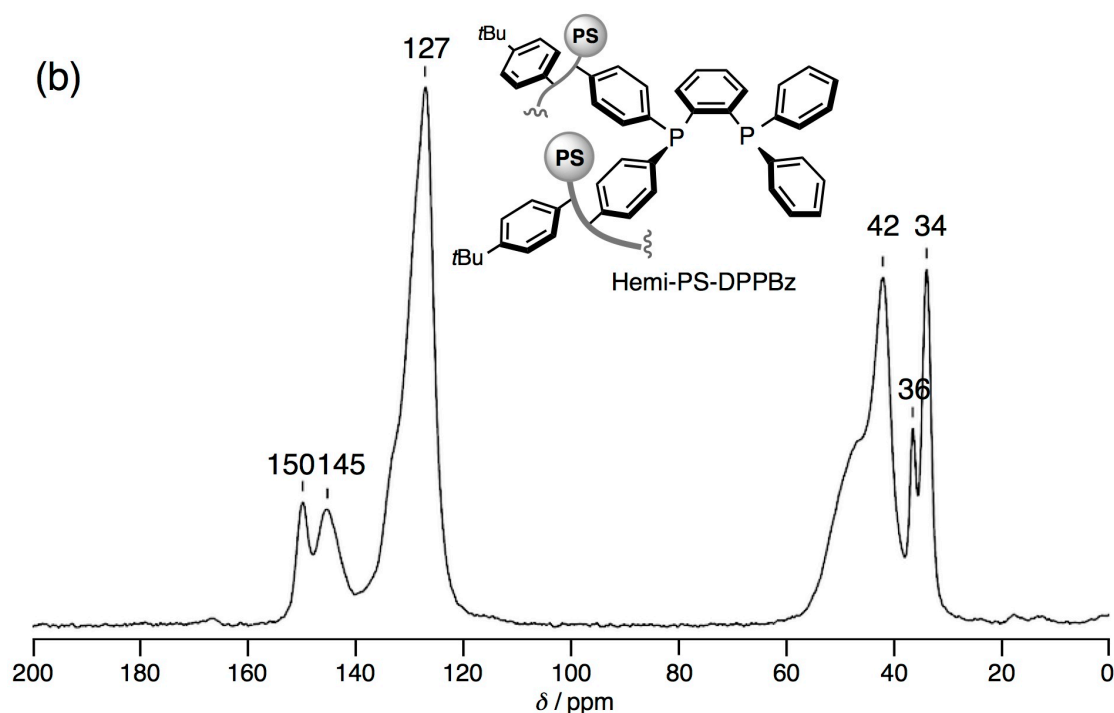


Figure 3 (a) ^{31}P CP/MAS and (b) ^{13}C CP/MAS NMR spectra of Hemi-PS-DPPBz.

5. Reactions of $\text{Ni}(\text{cod})_2$ and PS-DPPBz

All operations using $\text{Ni}(0)$ complexes were conducted in the N_2 -filled glove box due to unstability of $\text{Ni}(0)$ species.

The PS resin **1** ([P] 0.1 mmol/g, 200 mg, 0.02 mmol) and $[\text{Ni}(\text{cod})_2]$ (2.75 mg, 0.01 mmol or 11.0 mg, 0.04 mmol) were placed in a 5-mL vial tube. Anhydrous and degassed benzene (2 mL) was added to the tube, and the mixture was stirred at 60 °C for 0.5 h. The suspension was filtered with a glass pipette equipped with a cotton plug and washed with benzene. The red beads of the PS resin were dried under vacuum at room temperature for 15 min, and analyzed by ^{31}P CP/MAS NMR spectroscopy. When the beads was put in air, the color of beads changed from red to yellow.

^{31}P CP/MAS NMR (121.5 MHz): δ -17, 39.

6. Reaction of $\text{Ni}(\text{cod})_2$ and DPPBz

In a glove box, DPPBz (9 mg, 0.02 mmol), $\text{Ni}(\text{cod})_2$ (0.01 mmol for DPPBz/Ni 2:1, 0.02 mmol for DPPBz/Ni 1:1) were placed in NMR tube and dissolved in 1 mL of anhydrous and degassed C_6D_6 and stirred at 60 °C for 10 min, and analyzed by ^{31}P

NMR spectroscopy.

For Ni/DPPBz 1:1; ^{31}P NMR (161.8 MHz, C_6D_6): δ 48, 56.

For Ni/DPPBz 1:2; ^{31}P NMR (161.8 MHz, C_6D_6): δ -13, 48.

7. Preparations of Ni(cod)(DPPBz) and Ni(DPPBz)₂

Ni(cod)(DPPBz)

The mixture of DPPBz (45 mg, 0.1 mmol) and Ni(cod)₂ (29 mg, 0.105 mmol) in anhydrous and degassed benzene (2 mL) stirred at room temperature for 30 min. The residue was recrystallized from benzene/hexane to give Ni(cod)(DPPBz) as a orange solid (38 mg, 61% yield)

^1H NMR (400 MHz, C_6D_6): δ 2.17-2.45 (m, 8H), 4.33 (s, 4H), 6.80-6.86 (m, 2H), 7.03 (t, J = 7.2 Hz 4H), 7.10 (t, J = 7.2 Hz, 8H), 7.39-7.45 (m, 2H), 7.51-7.59 (m, 8H) ^{31}P NMR (161.8 MHz, C_6D_6): δ 55.8

Ni(DPPBz)₂

The mixture of DPPBz (90 mg, 0.2 mmol) and Ni(cod)₂ (28 mg, 0.1 mmol) in anhydrous and degassed benzene (2 mL) stirred at room temperature for 30 min. The residue was recrystallized from benzene/hexane to give Ni(DPPBz)₂ as a orange solid (68 mg, 71% yield)

^1H NMR (400 MHz, C_6D_6): δ 6.76-6.80 (m, 2H), 6.83 (t, J = 7.2 Hz, 8H), 6.92 (t, J = 7.2 Hz 4H), 7.31-7.39 (m, 8H), 7.39-7.44 (m, 2H) ^{31}P NMR (161.8 MHz, C_6D_6): δ 47.7

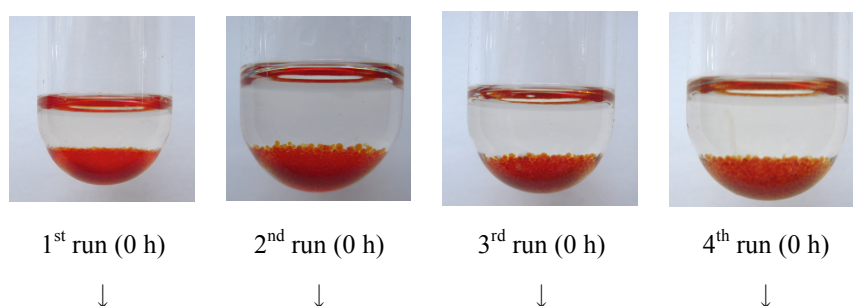
8. General Procedure for Ni-catalyzed Amination of Chloroarens

In a nitrogen-filled glove box, PS-DPPBz (38.3 mg, 0.00375 mmol), a solution of Ni(cod)₂ (0.69 mg, 0.0025 mmol) in anhydrous, degassed toluene (0.4 mL) and toluene (0.6 mL) were placed in a 10-mL glass tube containing a magnetic stirring bar. After stirring at room temperature for ca. 3 min, NaOtBu (36.0 mg, 0.375 mmol), 4-chloroanisole (**1a**, 31 μL , 35.6 mg, 0.25 mmol) and *n*-octylamine (**2a**, 62 μL , 48.5 mg, 0.375 mmol) were added successively. The tube was sealed with a screw cap and removed from the glove box. The mixture was stirred at 80 °C for 20 h. After it was cooled to room temperature, the mixture was diluted with Et₂O, and filtered through a Celite pad (eluting with EtOAc). The volatiles were removed under reduced pressure, and an internal standard (1,1,2,2-tetrachloroethane) was added to determine the yield of

4-methoxy-*N*-octylaniline (**3a**, >99% yield). The crude product was purified by silica gel chromatography (5:95 EtOAc/hexane) to give **3a** as pale yellow oil (52.1 mg, 0.22 mmol, 89% yield).

9. Reuse of Ni-PS-DPPBz System

In a nitrogen-filled glove box, PS-DPPBz (38.3 mg, 0.00375 mmol) and a solution of Ni(cod)₂ (0.69 mg, 0.0025 mmol) in anhydrous, degassed toluene (0.4 mL) and toluene (0.6 mL) were placed in a 10-mL glass tube containing a magnetic stirring bar. After stirring at room temperature for ca. 3 min, NaOtBu (36.0 mg, 0.375 mmol), *p*-chloroanisole (**1a**, 31 μ L, 35.6 mg, 0.25 mmol), and *n*-octylamine (**2a**, 62 μ L, 48.5 mg, 0.375 mmol) were added successively. The tube was sealed with a screw cap and removed from the glove box. The mixture was stirred at 100 °C for 10 h. After it was cooled to room temperature, the tube was placed inside the glove box. The red beads containing the Ni-PS-DPPBz catalyst were transferred to a new 10-mL glass tube containing a magnetic stirring bar, and the PS resin was washed with THF (2 mL x 2) and toluene (2 mL x 1), successively. The Ni-PS-DPPBz catalyst obtained in this manner was used for second run. Anhydrous, degassed toluene (1 mL), NaOtBu (36.0 mg, 0.375 mmol), **1a** (31 μ L, 35.6 mg, 0.25 mmol), **2a** (62 μ L, 48.5 mg, 0.375 mmol) were added, and the mixture was stirred at 100 °C for 10 h. The yields of **3a** were determined by ¹H NMR analysis with 1,1,2,2-tetrachloroethane as an internal standard. This recycling procedure was repeated five times (1st run, >99%; 2nd run, >99%; 3rd run, >99%; 4th run, 93%; 5th run, 40%). During the reuse test, gradual discoloring of the resins was observed probably due to Ni leaching into the solution phase (Figure 4).



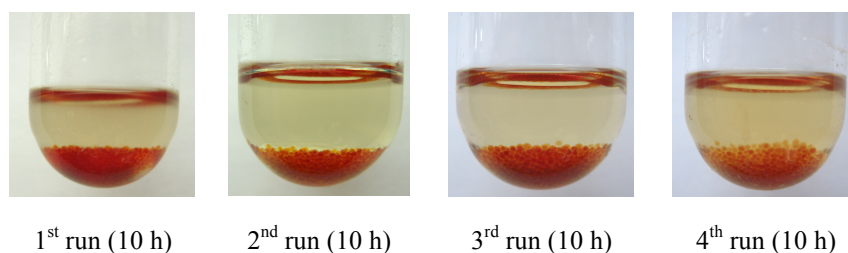


Figure 4. Photographic images of the reaction mixtures before (0 h) or after (10 h) the amination (1st–4th runs)

10. ICP-AES Measurement for Ni Residue

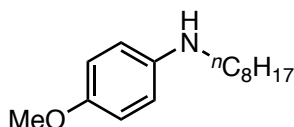
After the reaction between **1a** (0.25 mmol) and **2a** (0.375 mmol) in the presence of 1 mol% of the Ni-PS-DPPBz catalyst was conducted (100 °C, 10 h, in Scheme 2), the crude products containing 1,1,2,2-tetrachloroethane for ¹H NMR analysis were diluted with Et₂O, and filtered thorough a Celite pad (eluting with Et₂O). The volatiles were evaporated. A small aliquot of the residue was taken for a microwave-assisted acid digestion with aqua regia (1 mL, 1000 W, 220 °C). The resulting mixture was diluted in H₂O (50 mL). This solution was subjected to ICP-AES analysis.

Table 4. Detection of Ni leaching from Ni-PS-DPPBz by ICP-AES analysis

entry	Ni leaching (percentage of the loaded Ni, %)
1 st run	5.6
2 nd run	3.9
3 rd run	4.6
4 th run	4.0

Charaterization of Coupling Products

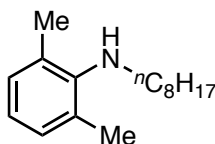
4-Methoxy-*N*-octylaniline (**3a**)



The product **3a** was isolated by silica gel chromatography (5% EtOAc/hexane). (52.1 mg, 89% yield). Pale yellow oil. ¹H NMR (400 MHz, CDCl₃): δ 0.88 (t, *J* = 6.8 Hz, 3H), 1.28–1.38 (m, 10H), 1.57 (quint, *J* = 8.0 Hz, 2H), 3.05 (t, *J* = 6.8 Hz, 2H), 3.22 (broad s, 1H), 3.74 (s, 3H), 6.58 (d, *J* = 9.0 Hz, 2H), 6.77 (d, *J* = 9.0 Hz, 2H). ¹³C NMR

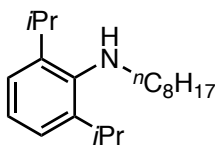
(100.5 MHz, CDCl₃): δ 14.07, 22.63, 27.17, 29.24, 29.41, 29.65, 31.80, 44.97, 55.77, 113.95 (2C), 114.82 (2C), 142.83, 151.88. **IR** (ATR): 3396, 2925, 2854, 1511, 1465, 1232, 816, 724 cm⁻¹. **EI-MS** (m/z): [M]⁺ calcd for C₁₅H₂₅ON, 235.1936; found, 235.

2,6-Dimethyl-*N*-octylaniline (3b)



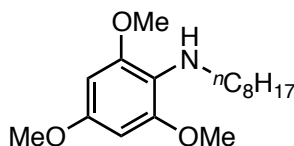
The product **3b** was isolated by silica gel chromatography (2% EtOAc/hexane). (56.4 mg, 97% yield). Colorless oil. **¹H NMR** (400 MHz, CDCl₃): δ 0.88 (t, J = 6.8 Hz, 3H), 1.28–1.40 (m, 10H), 1.57 (quint, J = 7.6 Hz, 2H), 2.28 (s, 6H), 2.96 (t, J = 7.6 Hz, 3H), 6.80 (t, J = 7.6 Hz, 1H), 6.98 (d, J = 7.6 Hz, 2H). **¹³C NMR** (100.5 MHz, CDCl₃): δ 14.08, 18.55 (2C), 22.63, 27.17, 29.27, 29.49, 31.21, 31.81, 48.66, 121.48, 128.74 (3C), 129.04, 146.43. **IR** (ATR): 2924, 2854, 1474, 761, 722 cm⁻¹. **EI-MS** (m/z): [M]⁺ calcd for C₁₆H₂₇N, 233.2143; found, 233.

2,6-Diisopropyl-*N*-octylaniline (3c)



The product **3c** was isolated by silica gel chromatography (3% EtOAc/hexane). (66.9 mg, 92% yield). Colorless oil. **¹H NMR** (400 MHz, CDCl₃): δ 0.89 (t, J = 6.4 Hz, 3H), 1.23–1.40 (m, 22H), 1.63 (quint, J = 6.8 Hz, 2H), 2.84–2.90 (m, 3H), 3.26 (septet, J = 6.8 Hz, 2H), 7.02–7.10 (m, 3H). **¹³C NMR** (100.5 MHz, CDCl₃): δ 14.10, 22.65, 24.26 (4C), 27.22, 27.64 (2C), 29.28, 29.51, 31.03, 31.84, 52.11, 123.46 (3C), 142.22 (2C), 143.69. **IR** (ATR): 2959, 2925, 2855, 1457, 1446, 754, 721 cm⁻¹. **HRMS-ESI** (m/z): [M + H]⁺ calcd for C₂₀H₃₆N, 290.28423 ; found, 290.28420.

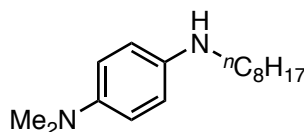
2,4,6-Trimethoxy-*N*-octylaniline (3d)



The product **3d** was isolated by silica gel chromatography (10% EtOAc/hexane). (58.8

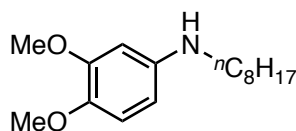
mg, 80% yield). Yellow oil. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 0.88 (t, $J = 6.4$ Hz, 3H), 1.27–1.35 (m, 10H), 1.49 (quint, $J = 7.6$ Hz, 2H), 3.05 (t, $J = 6.8$ Hz, 2H), 3.42 (broad s, 1H), 3.78 (s, 3H), 3.82 (s, 6H), 6.15 (s, 2H). $^{13}\text{C NMR}$ (100.5 MHz, CDCl_3): δ 14.05, 22.61, 27.00, 29.25, 29.41, 30.46, 31.78, 48.05, 55.44, 55.76 (2C), 91.24 (2C), 120.88, 152.15 (2C), 154.58. **IR** (ATR): 2924, 2853, 1601, 1501, 1456, 1202, 1115, 809, 731 cm^{-1} . **HRMS-ESI** (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{17}\text{H}_{30}\text{O}_3\text{N}$, 296.22202; found, 296.22220.

N^1, N^1 -Dimethyl- N^4 -octylbenzene-1,4-diamine (**3e**)



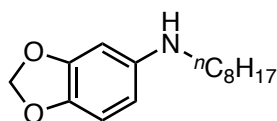
The product **3e** was isolated by silica gel chromatography (10–20% EtOAc/hexane). (42.6 mg, 69% yield). Pale yellow oil. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 0.88 (t, $J = 6.8$ Hz, 3H), 1.28–1.38 (m, 10H), 1.59 (quint, $J = 7.6$ Hz, 2H), 2.81 (s, 6H), 3.05 (broad s, 1H), 6.61 (d, $J = 8.0$ Hz, 2H), 6.74 (d, $J = 8.0$ Hz, 2H). $^{13}\text{C NMR}$ (100.5 MHz, CDCl_3): δ 14.10, 22.64, 27.21, 29.26, 29.43, 29.75, 31.82, 42.35 (2C), 45.11, 114.22 (2C), 115.98 (2C), 141.21, 143.95. **IR** (ATR): 2924, 2853, 1516, 1475, 1301, 1259, 1138, 946, 810, 722 cm^{-1} . **HRMS-ESI** (m/z): $[\text{M}]^+$ calcd for $\text{C}_{16}\text{H}_{28}\text{O}_2$, 248.22470; found, 248.22509.

3,4-Dimethoxy- N -octylaniline (**3f**)



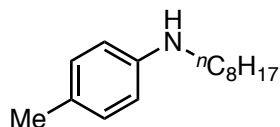
The product **3f** was isolated by silica gel chromatography (10% EtOAc/hexane). (60.9 mg, 92% yield). Brown oil. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 0.88 (t, $J = 6.4$ Hz, 3H), 1.28–1.40 (m, 10H), 1.61 (quint, $J = 7.2$ Hz, 2H), 3.06 (t, $J = 7.6$ Hz, 2H), 3.20 (broad s, 1H), 3.80 (s, 3H), 3.84 (s, 3H), 6.14 (dd, $J = 8.8, 2.8$ Hz, 1H), 6.24 (d, $J = 2.8$ Hz, 1H), 6.75 (d, $J = 8.8$ Hz, 2H). $^{13}\text{C NMR}$ (100.5 MHz, CDCl_3): δ 14.06, 22.62, 27.16, 29.21, 29.39, 29.62, 31.77, 44.82, 55.63, 56.66, 98.75, 103.36, 113.19, 141.29, 143.48. **IR** (ATR): 2925, 2854, 1513, 1464, 1229, 1209, 1026, 819, 730 cm^{-1} . **HRMS-ESI** (m/z): $[\text{M}]^+$ calcd for $\text{C}_{16}\text{H}_{28}\text{O}_2\text{N}$, 266.21146; found, 266.21144.

N-Octyl-1,3-benzodioxol-5-amine (3g)



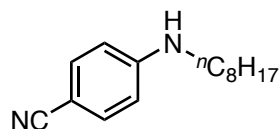
The product **3g** was isolated by silica gel chromatography (10% EtOAc/hexane). (54.6 mg, 88% yield). Pale yellow crystal. **¹H NMR** (400 MHz, CDCl₃): δ 0.88 (t, J = 7.2 Hz, 3H), 1.28–1.38 (m, 10H), 1.59 (quint, J = 7.6 Hz, 2H), 3.02 (t, J = 6.8 Hz, 2H), 3.32 (broad s, 1H), 5.84 (s, 2H), 6.04 (dd, J = 5.6, 3.2 Hz, 1H), 6.24 (d, J = 2.0 Hz, 1H), 6.65 (d, J = 8.4 Hz, 2H). **¹³C NMR** (100.5 MHz, CDCl₃): δ 14.08, 22.63, 27.16, 29.23, 29.39, 29.55, 31.80, 45.00, 95.78, 100.47, 104.21, 108.58, 139.32, 144.35, 148.27. **IR** (ATR): 3401, 2924, 2852, 1504, 1488, 1478, 1198, 1038, 939, 925, 810, 782, 729 cm⁻¹. **EI-MS** (m/z): [M]⁺ calcd for C₁₅H₂₃O₂N, 249.1729; found, 249.

4-Methyl-N-octylaniline (3h)



The product **3h** was isolated by silica gel chromatography (5% EtOAc/hexane). (43.3 mg, 80% yield). Pale yellow oil. **¹H NMR** (400 MHz, CDCl₃): δ 0.88 (t, J = 6.4 Hz, 3H), 1.28–1.40 (m, 10H), 1.60 (quint, J = 6.4 Hz, 2H), 2.23 (s, 3H), 3.07 (t, J = 7.2 Hz, 2H), 3.39 (broad s, 1H), 6.52 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 7.6 Hz, 2H). **¹³C NMR** (100.5 MHz, CDCl₃): δ 14.09, 20.36, 22.65, 27.18, 29.26, 29.41, 29.59, 31.82, 44.37, 112.87 (2C), 126.25, 129.67 (2C), 146.28. **IR** (ATR): 3382, 2920, 2852, 1619, 1521, 1468, 808, 726 cm⁻¹. **EI-MS** (m/z): [M]⁺ calcd for C₁₅H₂₅N, 219.1987; found, 219.

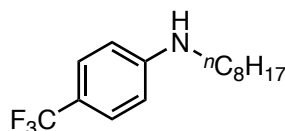
4-(Octylamino)-benzonitrile (3i)



The product **3i** was isolated by silica gel chromatography (10% EtOAc/hexane). (51.7 mg, 90% yield). White crystal. **¹H NMR** (400 MHz, CDCl₃): δ 0.88 (t, J = 6.4 Hz, 3H), 1.28–1.39 (m, 10H), 1.62 (quint, J = 7.2 Hz, 2H), 3.13 (t, J = 6.8 Hz, 2H), 4.22 (broad s, 1H), 6.54 (d, J = 5.2 Hz, 2H), 7.40 (d, J = 6.8 Hz, 2H). **¹³C NMR** (100.5 MHz, CDCl₃):

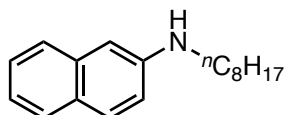
δ 14.04, 22.59, 26.97, 29.08, 29.16, 29.25, 31.73, 43.16, 98.14, 111.95 (2C), 120.57, 133.63 (2C), 151.41. **IR** (ATR): 3372, 2925, 2858, 2206, 1603, 1525, 1478, 1345, 1170, 824, 724 cm^{-1} . **EI-MS** (m/z): $[\text{M}]^+$ calcd for $\text{C}_{15}\text{H}_{22}\text{N}_2$, 230.1783; found, 230.

***N*-Octyl-4-(trifluoromethyl)-aniline (3j)**



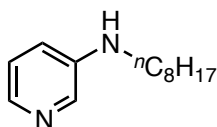
The product **3j** was isolated by silica gel chromatography (1% EtOAc/hexane). (63.6 mg, 93% yield). Pale yellow oil. **^1H NMR** (400 MHz, CDCl_3): δ 0.89 (t, J = 6.4 Hz, 3H), 1.28–1.39 (m, 10H), 1.61 (quint, J = 7.6 Hz, 2H), 3.12 (t, J = 6.8 Hz, 2H), 3.93 (broad s, 1H), 6.57 (d, J = 8.8 Hz, 2H), 7.38 (d, J = 8.8 Hz, 2H). **^{13}C NMR** (100.5 MHz, CDCl_3): δ 14.07, 22.64, 27.07, 29.23, 29.29, 29.35, 31.80, 43.50, 111.61 (2C), 118.35 (q, $J_{\text{C-F}}$ = 32.6 Hz), 125.05 (q, $J_{\text{C-F}}$ = 270.2 Hz), 126.57 (2C), 150.85. **IR** (ATR): 3372, 2925, 2858, 2206, 1603, 1525, 1478, 1345, 1170, 824, 724 cm^{-1} . **EI-MS** (m/z): $[\text{M}]^+$ calcd for $\text{C}_{15}\text{H}_{22}\text{F}_3\text{N}$, 273.1704; found, 273.

***N*-Octyl-2-naphthalenamine (3k)**



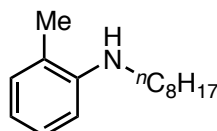
The product **3k** was isolated by silica gel chromatography (3–5% EtOAc/hexane). (61.2 mg, 96% yield). Yellow oil. **^1H NMR** (400 MHz, CDCl_3): δ 0.89 (t, J = 6.8 Hz, 3H), 1.29–1.40 (m, 10H), 1.64 (quint, J = 8.0 Hz, 2H), 3.18 (t, J = 6.8 Hz, 2H), 3.74 (broad s, 1H), 6.78 (d, J = 2.4 Hz, 1H), 6.84 (dd, J = 8.8, 2.4 Hz), 7.17 (dt, J = 8.0, 0.8 Hz, 1H), 7.34 (dt, J = 6.8, 1.6 Hz, 1H), 7.60 (d, J = 9.2 Hz, 2H), 7.65 (d, J = 8.0 Hz, 1H). **^{13}C NMR** (100.5 MHz, CDCl_3): δ 14.10, 22.65, 27.22, 29.26, 29.38, 29.41, 31.82, 43.98, 104.09, 117.95, 121.73, 125.82, 126.22, 127.32, 127.58, 128.78, 135.26, 146.11. **IR** (ATR): 3412, 2924, 2853, 1629, 1604, 1521, 1467, 825, 804, 741 cm^{-1} . **EI-MS** (m/z): $[\text{M}]^+$ calcd for $\text{C}_{18}\text{H}_{25}\text{N}$, 255.1987; found, 255.

***N*-Octylpyridine-3-amine (3l)**



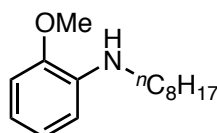
The product **3l** was isolated by silica gel chromatography (30% EtOAc/hexane). (48.5 mg, 94% yield). White crystal. ^1H NMR (400 MHz, CDCl_3): δ 0.89 (t, $J = 6.8$ Hz, 3H), 1.28–1.40 (m, 10H), 1.62 (quint, $J = 7.6$ Hz, 2H), 3.10 (q, $J = 6.8$ Hz, 2H), 3.74 (broad s, 1H), 6.85 (dt, $J = 2.8, 1.6$ Hz, 1H), 7.07 (dd, $J = 8.0, 4.4$ Hz, 1H), 7.93 (dd, $J = 4.8, 1.6$ Hz, 1H), 8.02 (d, $J = 2.4$ Hz, 1H). ^{13}C NMR (100.5 MHz, CDCl_3): δ 14.03, 22.58, 27.01, 29.17, 29.30 (2C), 31.73, 43.49, 118.15, 123.61, 135.91, 138.36, 144.34. IR (ATR): 3257, 2955, 2926, 2851, 1584, 1533, 1476, 1418, 1319, 1245, 789, 704 cm^{-1} . EI-MS (m/z): $[\text{M}]^+$ calcd for $\text{C}_{13}\text{H}_{22}\text{N}_2$, 206.1783; found, 206.

2-Methyl-*N*-Octylaniline (**3m**)



The product **3m** was isolated by silica gel chromatography (5% EtOAc/hexane). (56.8 mg, 97% yield). Pale yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 0.89 (t, $J = 6.4$ Hz, 3H), 1.28–1.45 (m, 10H), 1.66 (quint, $J = 7.2$ Hz, 2H), 2.13 (s, 3H), 3.14 (t, $J = 7.6$ Hz, 2H), 3.42 (broad s, 1H), 6.59–6.65 (m, 2H), 7.04 (d, $J = 6.8$ Hz, 1H), 7.12 (t, $J = 8.0$ Hz, 1H). ^{13}C NMR (100.5 MHz, CDCl_3): δ 14.10, 17.43, 22.65, 27.23, 29.26, 29.42, 29.59, 31.83, 43.93, 109.53, 116.54, 121.61, 127.10, 129.96, 146.37. IR (ATR): 3431, 2924, 2854, 1607, 1513, 743, 714 cm^{-1} . EI-MS (m/z): $[\text{M}]^+$ calcd for $\text{C}_{15}\text{H}_{25}\text{N}$, 219.1987; found, 219.

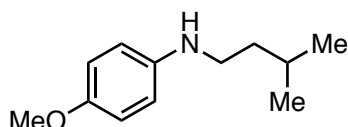
2-Methoxy-*N*-octylaniline (**3n**)



The product **3n** was isolated by silica gel chromatography (5% EtOAc/hexane). (54.6 mg, 93% yield). Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 0.88 (t, $J = 7.2$ Hz, 3H), 1.28–1.41 (m, 10H), 1.65 (quint, $J = 8.0$ Hz, 2H), 3.10 (t, $J = 7.2$ Hz, 2H), 3.83 (s, 3H), 4.16 (broad s, 1H), 6.59–6.65 (m, 2H), 6.75 (dd, $J = 7.6, 1.2$ Hz, 1H), 6.86 (dt, $J = 8.0,$

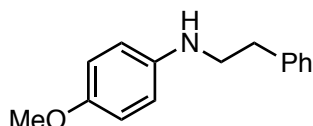
1.6 Hz, 1H). ^{13}C NMR (100.5 MHz, CDCl_3): δ 14.09, 22.65, 27.23, 29.25, 29.42, 29.51, 31.83, 43.69, 55.32, 109.23, 109.67, 116.01, 121.24, 138.46, 146.66. IR (ATR): 3427, 2925, 2854, 1603, 1512, 1456, 1245, 1220, 730 cm^{-1} . EI-MS (m/z): $[\text{M}]^+$ calcd for $\text{C}_{15}\text{H}_{25}\text{ON}$, 235.1936; found, 235.

4-Methoxy-*N*-(3-methylbutyl)-aniline (**3o**)



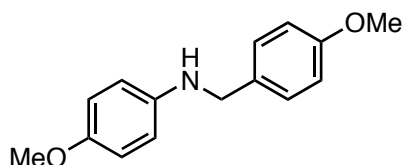
The product **3o** was isolated by silica gel chromatography (5% EtOAc/hexane). (37.4 mg, 77% yield). Brown oil. ^1H NMR (400 MHz, CDCl_3): δ 0.94 (t, $J = 6.4$ Hz, 6H), 1.50 (q, $J = 6.8$ Hz, 2H), 1.69 (septet, $J = 6.8$ Hz, 1H), 3.07 (t, $J = 7.2$ Hz, 2H), 3.28 (broad s, 1H), 3.75 (s, 3H), 6.58 (d, $J = 6.4$ Hz, 2H), 6.78 (d, $J = 9.2$ Hz, 2H). ^{13}C NMR (100.5 MHz, CDCl_3): δ 22.62 (2C), 26.00, 38.68, 43.14, 55.81, 113.99 (2C), 114.84 (2C), 142.85, 151.92. IR (ATR): 3394, 2954, 1509, 1232, 1037, 816 cm^{-1} . EI-MS (m/z): $[\text{M}]^+$ calcd for $\text{C}_{12}\text{H}_{19}\text{ON}$, 194.1467; found, 193.

4-Methoxy-*N*-phenethylaniline (**3p**)



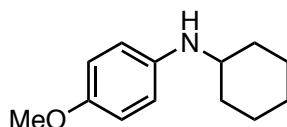
The product **3p** was isolated by silica gel chromatography (5–10% EtOAc/hexane). (53.7 mg, 94% yield). Yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 2.90 (t, $J = 7.2$ Hz, 2H), 3.35 (t + broad s, $J = 6.8$ Hz, 2H + 1H), 3.74 (s, 3H), 6.58 (d, $J = 9.2$ Hz, 2H), 6.78 (d, $J = 9.2$ Hz, 2H), 7.20–7.33 (m, 5H). ^{13}C NMR (100.5 MHz, CDCl_3): δ 35.52, 45.97, 55.73, 114.32 (2C), 114.84 (2C), 126.33, 128.53 (2C), 128.74 (2C), 139.35, 142.16, 152.10. IR (ATR): 3393, 3027, 2933, 2831, 1509, 1232, 1035, 818, 747, 699 cm^{-1} . EI-MS (m/z): $[\text{M}]^+$ calcd for $\text{C}_{15}\text{H}_{17}\text{ON}$, 227.1310; found, 227.

4-Methoxy-*N*-(4-methoxybenzyl)aniline (**3q**)



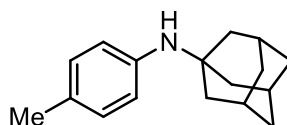
The product **3q** was isolated by silica gel chromatography (10% EtOAc/hexane). (58.3 mg, 96% yield). White crystal. **¹H NMR** (400 MHz, CDCl₃): δ 3.72 (s + broad s, 3H + 1H), 3.78 (s, 3H), 4.19 (s, 2H), 6.59 (d, J = 9.2 Hz, 2H), 6.77 (d, J = 9.2 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 7.27 (d, J = 8.8 Hz, 2H). **¹³C NMR** (100.5 MHz, CDCl₃): δ 48.62, 55.21, 55.72, 113.89 (2C), 114.02 (2C), 114.80 (2C), 128.75 (2C), 131.60, 142.46, 152.05, 158.71. **IR** (ATR): 3374, 3013, 2952, 2907, 2837, 1609, 1511, 1247, 1029, 821, 733 cm⁻¹. **EI-MS** (m/z): [M]⁺ calcd for C₁₅H₁₇O₂N, 243.1259; found, 243.

***N*-Cyclohexyl-4-methoxyaniline (3r)**



The product **3r** was isolated by silica gel chromatography (5% EtOAc/hexane). (48.2 mg, 94% yield). Yellow crystal. **¹H NMR** (400 MHz, CDCl₃): δ 1.06–1.40 (m, 5H), 1.62–1.67 (m, 1H), 1.72–1.77 (m, 2H), 2.02–2.06 (m, 2H), 3.12–3.19 (m, 2H), 3.74 (s, 3H), 6.57 (d, J = 9.2 Hz, 2H), 6.76 (d, J = 8.8 Hz, 2H). **¹³C NMR** (100.5 MHz, CDCl₃): δ 25.04 (2C), 25.94, 33.59 (2C), 52.72, 55.76, 114.75 (2C), 114.84 (2C), 141.57, 151.77. **IR** (ATR): 2929, 2838, 1512, 1457, 1242, 1029, 820, 733 cm⁻¹. **EI-MS** (m/z): [M]⁺ calcd for C₁₃H₂₉ON, 205.1467; found, 205.

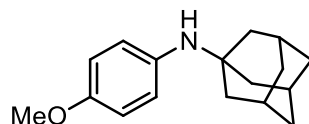
***N*-(4-Methylphenyl)-1-adamantanamine (3s)**



The product **3s** was isolated by silica gel chromatography (2% EtOAc/hexane). (50.1 mg, 83% yield). White crystal. **¹H NMR** (400 MHz, CDCl₃): δ 1.61–1.69 (m, 6H), 1.81 (d, J = 2.8 Hz, 6H), 2.09 (s, 3H), 2.25 (s, 3H), 3.03 (broad s, 1H), 6.74 (d, J = 8.8 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H). **¹³C NMR** (100.5 MHz, CDCl₃): δ 20.53, 29.71 (3C), 36.46 (3C), 43.62 (3C), 52.33, 120.81 (2C), 129.18 (2C), 129.36, 143.09. **IR** (ATR):

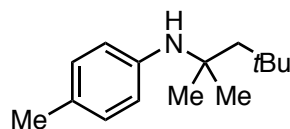
3410, 2908, 2849, 1610, 1515, 1308, 803 cm^{-1} . **EI-MS** (m/z): $[\text{M}]^+$ calcd for $\text{C}_{17}\text{H}_{23}\text{N}$, 241.1830; found, 241.

***N*-(4-Methoxyphenyl)-1-adamantanamine (3t)**



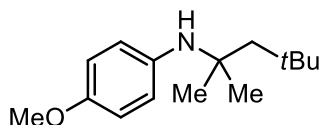
The product **3t** was isolated by silica gel chromatography (5% EtOAc/hexane). (49.8 mg, 77% yield). Pale yellow crystal. **^1H NMR** (400 MHz, CDCl_3): δ 1.63 (q, J = 12.4 Hz, 6H), 1.74 (d, J = 2.8 Hz, 6H), 2.08 (s, 3H), 2.77 (broad s, 1H), 3.76 (s, 3H), 6.74–6.77 (m, 2H), 6.82–6.84 (m, 2H). **^{13}C NMR** (100.5 MHz, CDCl_3): δ 29.81 (3C), 36.41 (3C), 43.67 (3C), 52.55, 55.39, 113.77 (2C), 124.22 (2C), 138.23, 154.75. **IR** (ATR): 3300, 2902, 2848, 1509, 1231, 1038, 835, 745 cm^{-1} . **EI-MS** (m/z): $[\text{M}]^+$ calcd for $\text{C}_{17}\text{H}_{23}\text{ON}$, 257.1780; found, 257.

4-Methyl-*N*-(1,1,3,3-tetramethylbutyl)-aniline (3u)



The product **3u** was isolated by silica gel chromatography (0–5% EtOAc/hexane). (46.2 mg, 84% yield). Pale yellow oil. **^1H NMR** (400 MHz, CDCl_3): δ 1.02 (s, 9H), 1.35 (s, 6H), 1.66 (s, 2H), 2.23 (s, 3H), 3.38 (broad s, 1H), 6.63 (d, J = 8.4 Hz, 2H), 6.95 (d, J = 7.6 Hz, 2H). **^{13}C NMR** (100.5 MHz, CDCl_3): δ 20.37, 30.36 (2C), 31.65 (3C), 31.75, 53.52, 55.22, 117.51 (2C), 127.01, 129.33 (2C), 114.32. **IR** (ATR): 2952, 2868, 1617, 1514, 1473, 1223, 909, 807, 731 cm^{-1} . **HRMS-ESI** (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{26}\text{N}$, 220.20598; found, 220.20564.

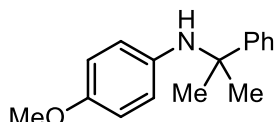
4-Methoxy-*N*-(1,1,3,3-tetramethylbutyl)-aniline (3v)



The product **3v** was isolated by silica gel chromatography (5% EtOAc/hexane). (41.1 mg, 84% yield). Yellow oil. **^1H NMR** (400 MHz, CDCl_3): δ 1.03 (s, 9H), 1.29 (s, 6H),

1.61 (s, 2H), 3.75 (s, 3H), 6.71–6.76 (m, 4H). ^{13}C NMR (100.5 MHz, CDCl_3): δ 30.09 (2C), 31.73 (4C), 54.32, 55.54, 55.75, 114.15 (2C), 121.10 (2C), 140.06, 153.35. IR (ATR): 2950, 2904, 1508, 1465, 1237, 1222, 1039, 819, 791 cm^{-1} . HRMS-ESI (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{26}\text{ON}$, 236.20089; found, 236.20118.

***N*-(4-Methoxyphenyl)- α,α -dimethylbenzylamine (3w)**



The product **3w** was isolated by silica gel chromatography (2–5% EtOAc/hexane). (39.6 mg, 66% yield). Yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 1.59 (s, 6H), 3.66 (s, 3H), 6.28–6.32 (m, 2H), 6.58–6.61 (m, 2H), 7.22–7.24 (m, 1H), 7.31–7.34 (m, 2H), 7.51–7.53 (m, 2H). ^{13}C NMR (100.5 MHz, CDCl_3): δ 30.61 (2C), 55.57, 55.99, 114.26 (2C), 117.10 (2C), 125.68 (2C), 126.25, 128.43 (2C), 140.08, 147.83, 152.02. IR (ATR): 3393, 2975, 2831, 1508, 1443, 1232, 1178, 1036, 820, 758, 700 cm^{-1} . HRMS-ESI (m/z): $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{20}\text{ON}$, 242.15394; found, 242.15418.

Reference and Notes

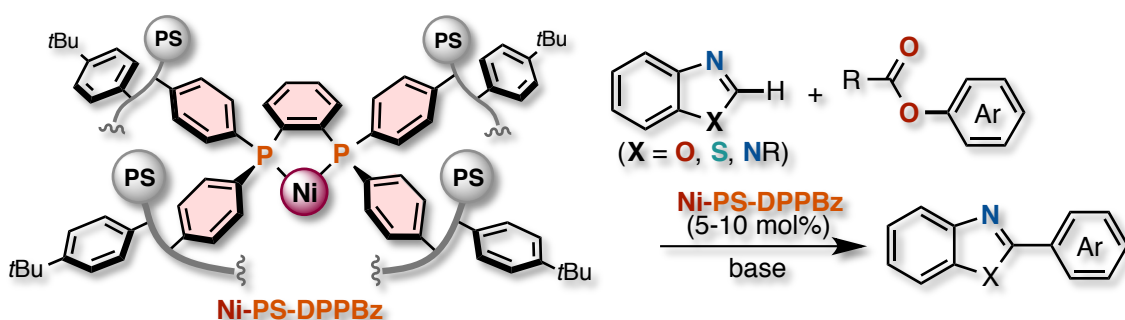
- (1) For a recent review on transition-metal catalyzed C–N coupling reactions, see; (a) Hartwig, J. F. *Acc. Chem. Res.* **2008**, *41*, 1534–1544.
- (2) For recent reviews of Ni catalysis, see: (a) Anaikov, V. P.; *ACS Catal.* **2015**, *5*, 1964–1971. (b) Tasker, S. Z.; Standley, E. A.; Jamison, T. F. *Nature* **2014**, *509*, 299–309.
- (3) Ge, S.; Green, R. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 1617–1627.
- (4) For selected reports of Ni-catalyzed amination of chloroarenes with primary alkylamines, see: (a) Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 6054–6058. (b) Desmarets, C.; Schneider, R.; Fort, Y. *J. Org. Chem.* **2002**, *67*, 3029–3036. (c) Kampmann, S.; Skelton, B. W.; Wild, D. A.; Koutsantonis, G. A.; Stewart, S. G. *Eur. J. Org. Chem.* **2015**, *2015*, 5995–6004.
- (5) Ni-catalyzed amination of chloroarenes with ammonia or ammonium salts using Josiphos-type ligands were reported: (a) Borzenko, A.; Rotta-Loria, N. L.; MacQueen, P. M.; Lavoie, C. M.; McDonald, R.; Strdiotto, M. *Angew. Chem., Int. Ed.* **2015**, *54*, 3773–3777. (b) Green, R. A.; Hartwig, J. F. *Angew. Chem., Int. Ed.*

2015, *54*, 3768–3772.

- (6) Cu-catalyzed amination of chloroarenes with primary and secondary amines was reported. Zhou, W.; Fan, M.; Yin, J.; Jiang, Y.; Ma, D. *J. Am. Chem. Soc.* **2015**, *137*, 11942–11945.
- (7) Iwai, T.; Harada, T.; Hara, K.; Sawamura, M. *Angew. Chem., Int. Ed.* **2013**, *125*, 12546–12552.
- (8) Homopolymer of tetravinylated bisphosphines; Sun, Q.; Dai, Z.; Liu, X.; Sheng, N.; Deng, F.; Meng, X.; Xiao, F.-S. *J. Am. Chem. Soc.* **2015**, *137*, 5204–5209.
- (9) Metal-organic frameworks with a DPPBz scaffold: Bohnsack, A. M.; Ibarra, I. A.; Bakmutov, V. I.; Lynch, V. M.; Humphrey, S. M.; *J. Am. Chem. Soc.* **2013**, *135*, 16038–16041.
- (10) For selected examples of tetravinylated bisphosphines as a multifold cross-linker for molecular imprinting, see: (a) Brunkan, N. M.; Gagné, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 6217–6225. (b) Voshell, S. M.; Gagné, M. R. *Organometallics* **2005**, *24*, 6338–6350.
- (11) Coordination property of PS-DPPBz toward Rh^I and Pd^{II} complex was discussed in chapter 2.
- (12) For selected examples of related works using sophisticated polymer-supported phosphine ligands, see: (a) Hu, Q.-S.; Lu, Y.; Tang, Z.-Y.; Yu, H.-B. *J. Am. Chem. Soc.* **2003**, *125*, 2856–2857. (b) Lu, Y.; Plocher, E.; Hu, Q.-S. *Adv. Synth. Catal.* **2006**, *348*, 841–845. (c) Akai, Y.; Yamamoto, T.; Nagata, Y.; Ohmura, T.; Sugimoto, M. *J. Am. Chem. Soc.* **2012**, *134*, 11092–11095.
- (13) (a) Falkowski, J. M.; Sawano, T.; Zhang, T.; Tsun, G.; Chen, Y.; Lockard, J. V.; Lin, W. *J. Am. Chem. Soc.* **2014**, *136*, 5213–5216. (b) Sawano, T.; Thacker, N. C.; Lin, Z.; McIsaac, A. R.; Lin, W. *J. Am. Chem. Soc.* **2015**, *137*, 12241–12248.
- (14) Hartwig reported that the reaction of 3-chloroanisole with *t*-butylamines or *t*-amylamines using Ni(BINAP)(*h*²-NC-Ph) catalyst system gave trace amount of the coupling products. See ref 3.
- (15) For a Pd catalyst, see: Ruiz-Castillo, P.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2015**, *137*, 3085–3092, references cited therein.

Chapter 4

Ni-(PS-DPPBz)-Catalyzed Direct C–H Arylation of 1,3-Azoles with Aryl Pivalates

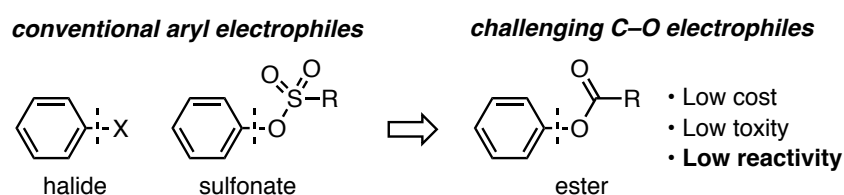


Abstract; Use of a bisphosphine-branched polystyrene PS-DPPBz enabled the Ni-catalyzed direct C–H arylation of 1,3-azoles with aryl pivalates, irrespective of the moderate electronic and steric nature of the 1,2-bis(diphenylphosphino)benzene-type ligand. The Ni-PS-DPPBz system was applicable to simple phenolic esters, for which reported protocols were not efficient, to give the C2-arylated azoles in good to high yields

Introduction

Phenol derivatives are attractive alternatives to aryl halides as electrophiles in transition-metal-catalyzed cross-coupling reactions owing to their broad availability and low toxicity (Scheme 1)¹. Aryl sulfonates such as aryl triflates have been conventionally used for this purpose because of their high reactivity toward the C(aryl)–O oxidative addition. In contrast, the use of aryl esters and their derivatives, which are much less expensive, toxic and reactive than triflates, as C–O electrophiles are still challenging².

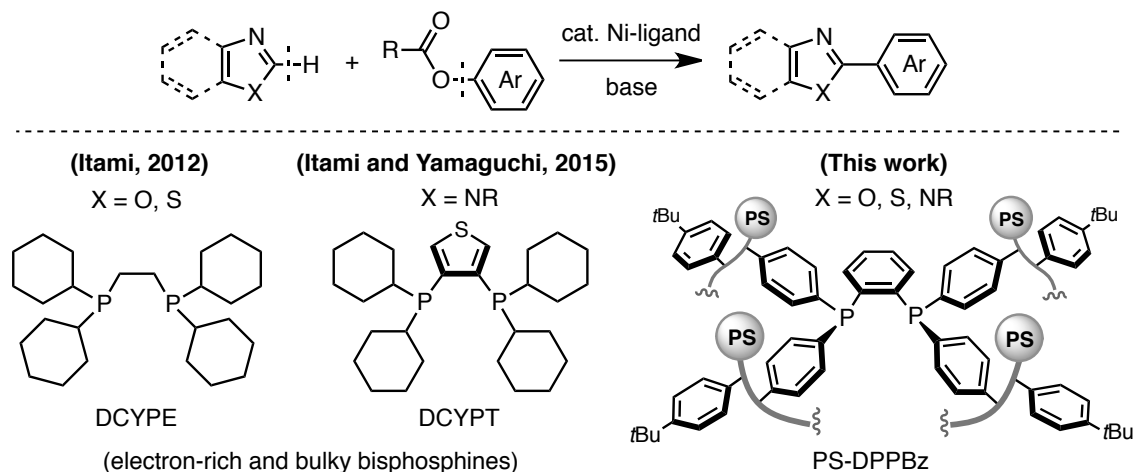
Scheme 1. Aryl electrophiles for transition-metal-catalyzed cross-coupling reactions.



Direct C–H arylation of heteroarenes with aryl electrophiles are a powerful method for synthesis of heterobiaryls³, which are common structures in natural products, pharmaceuticals, and functional materials. In 2012, Itami and coworkers reported an elegant Ni catalyst system for the C–H arylation of 1,3-azoles with phenol derivatives such as aryl esters, carbamates and carbonates in the presence of weak base^{5a}. The effects of ligands are crucial, and an electron-rich and bulky bisphosphine 1,2-bis(dicyclohexylphosphino)ethane (DCYPE) is a specifically efficient ligand to promote this Ni catalysis (Scheme 2). The strongly electron-donating DCYPE ligand can assist oxidative addition of the less reactive C(aryl)–O bonds to the Ni(0)-bisphosphine species. Additionally, the steric demand of cyclohexyl substituents on the P atoms increases stability of the resulting Ar–Ni(II)–OR species⁵. Later, Itami and Yamaguchi reported that 3,4-bis(dicyclohexylphosphino)thiophene (DCYPT) was also an effective ligand for the Ni-catalyzed direct C–H arylation of imidazoles with aryl carbamates^{4d} (Scheme 2). On the other hand, we recently developed a bisphosphine-branched polystyrene PS-DPPBz, and showed mono-ligating properties to various metals in Chapter 2. As described in Chapter 3, the heterogeneous Ni-PS-DPPBz system exhibited high catalytic efficiency for the amination of chloroarenes with primary alkylamines owing to polymer effects for effective site isolation of bisphosphine-bound active Ni species. On the basis of these knowledge, we

envisioned that an active Ni(0)-bisphosphine species for the C–H arylation of azoles with aryl esters as C–O electrophiles could be formed by using PS-DPPBz (Scheme 2).

Scheme 2. Ni-Catalyzed direct C–H arylation of azoles with C–O electrophiles.

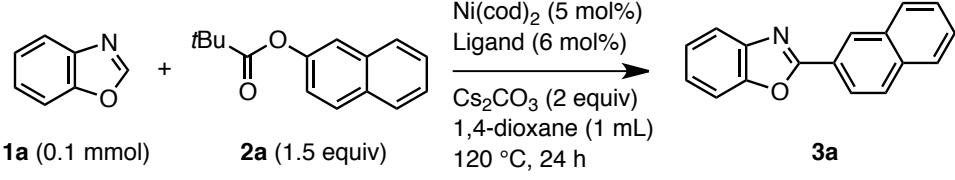


Herein, we reported that a bisphosphine-branched polystyrene PS-DPPBz enabled the Ni-catalyzed direct C–H arylation of 1,3-azoles with aryl esters. The Ni-PS-DPPBz system was applicable to more challenging electrophiles such as simple phenolic esters, for which the reported protocol with DCYPE was not efficient.

Results and Discussion

Various ligands were evaluated for their performances in the Ni-catalyzed direct C–H arylation of benzoxazole (**1**, 0.1 mmol) with 2-naphthyl pivalate (**2a**, 0.15 mmol) in the presence of Ni(cod)₂ as a metal precursor (5 mol%) and Cs₂CO₃ (0.2 mmol) as base in 1,4-dioxane at 120 °C for 24 h. The results are summarized in Table 1. As described by Itami et al., a *peralkylated* bisphosphine DCYPE effectively promoted the Ni catalysis to give the C-2 arylated benzoxazole **3a** quantitatively (entry 1). In contrast, a *perarylated* bisphosphine DPPBz with a rigid ortho-phenylene linker to connect two P atoms was not effective at all (entries 2). No reaction occurred with BINAP and DPPF, which were used in other Ni-catalyzed transformations of aryl pivalates^{2f,j} (entries 3 and 4). To our delight, a bisphosphine-branched polystyrene PS-DPPBz induced catalytic activity to afford **3a** in 82% yield (entry 5). These results suggested that strong electron-donation and steric hindrance was not necessary for ligands to promote the Ni catalysis.

Table 1. Ligand effects in the Ni-catalyzed direct C–H arylation of **1a** with **2a**.

 1a (0.1 mmol) 2a (1.5 equiv) 3a		
entry	ligand	Yield of 3a (%)
1	DCYPE	>99
2	DPPBz	0
3	BINAP	0
4	DPPF	0
5	PS-DPPBz	82 (78)
6	Hemi-PS-DPPBz	20
7	PS-DPPE	0
8	PS-TPP	0

Conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), Ni(cod)₂ (5 mol%), ligand (6 mol%), Cs₂CO₃, (0.2 mmol), 1,4-dioxane (1 mL), 120 °C, 24 h. Yields were determined by ¹H NMR analysis. The isolated yield is given in parenthesis.

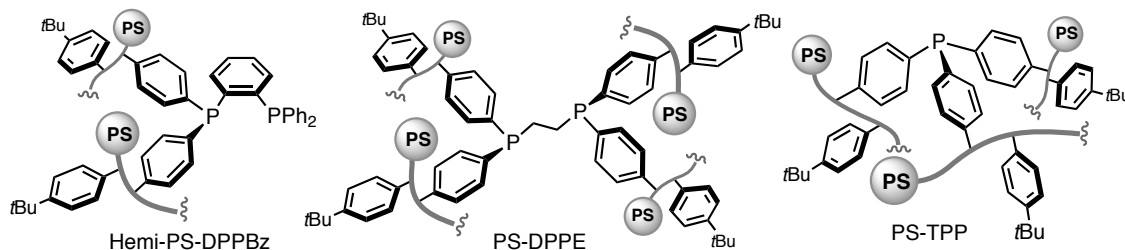
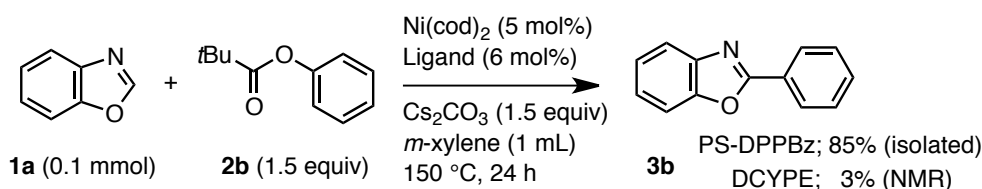


Table 1 also shows the effects of other bisphosphine- and monophosphine-cross-linked polystyrenes. A twofold cross-linking bisphosphine Hemi-PS-DPPBz promoted the coupling reaction (entry 6), but its reaction efficacy was much less than that of PS-DPPBz. PS-DPPE with a 1,2-bis(diphenylphosphino)ethane scaffold did not showed any activity (entry 7). No reaction occurred with the PPh₃-based ligand PS-TPP (entry 8). These results indicated that the fourfold-cross-linking of the DPPBz core is crucial for the high catalytic activity owing to the efficient site isolation of the bisphosphine-chelate Ni complexes in the polymer

matrix.

A significant advance of PS-DPPBz over DCYPE was found in the C–H arylation with simple phenol-derived esters, which are challenging electrophile compared to naphthol-based (π -extended) ones^{ref}. As shown in Scheme 3, the Ni-PS-DPPBz system efficiently catalyzed the direct C–H arylation of **1a** with phenyl pivalate (**1b**) in *m*-xylene at 150 °C to afford the desired product **3b** in 85% isolated yield. On the other hand, the use of DCYPE under otherwise same conditions was much less efficient⁸.

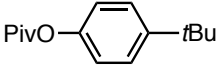
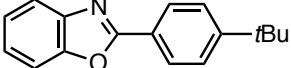
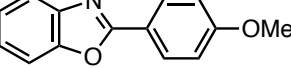
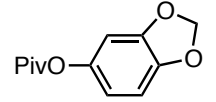
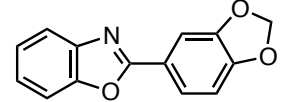
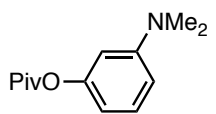
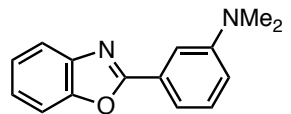
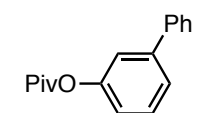
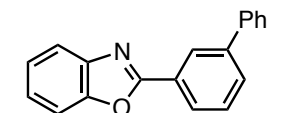
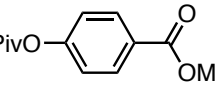
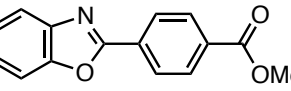
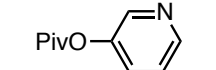
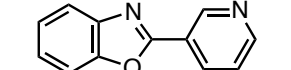
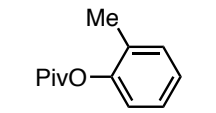
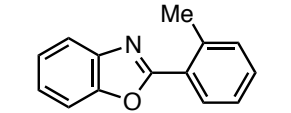
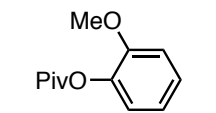
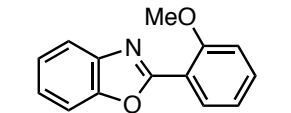
Scheme 3. The Ni-catalyzed C–H arylation of **1a** with **2b**



Various phenolic pivalates (**2**) reacted with **1a** in the presence of the Ni-PS-DPPBz system, as shown in Table 2. Electron-rich (**2c–2f**, entries 1–4), electron-neutral (**2g**, entry 5) and electron-deficient (**2h**, entry 6) aryl pivalates successfully participated in this transformation with 5–10 mol% of the Ni loading, affording the corresponding heterobiaryls **3c–3h** in moderate to high yields (44–94%). Notably, methyl ester was compatible under the mild basic conditions. The reaction with 3-pyridine pivalate (**2i**) proceeded in 1,4-dioxane at 120 °C to give 2-pyridylazole **3i** (entry 7). *Ortho*-substituted aryl pivalates such **2j** and **2k** were also suitable electrophiles for the coupling to provide sterically congested heterobiaryl **3j** and **3k** in useful yields (entries 8 and 9).

Table 2. Ni-catalyzed C-H/C-O coupling of various aryl pivalates^a,

entry	Aryl pivalate	2	Product	3	Yield (%) ^b

1 ^c		2c		3c	94
2		2d		3d	62
3		2e		3e	44
4		2f		3f	75
5		2g		3g	50
6 ^d		2h		3h	51
7 ^{c,e}		2i		3i	56
8		2j		3j	68
9 ^c		2k		3k	56

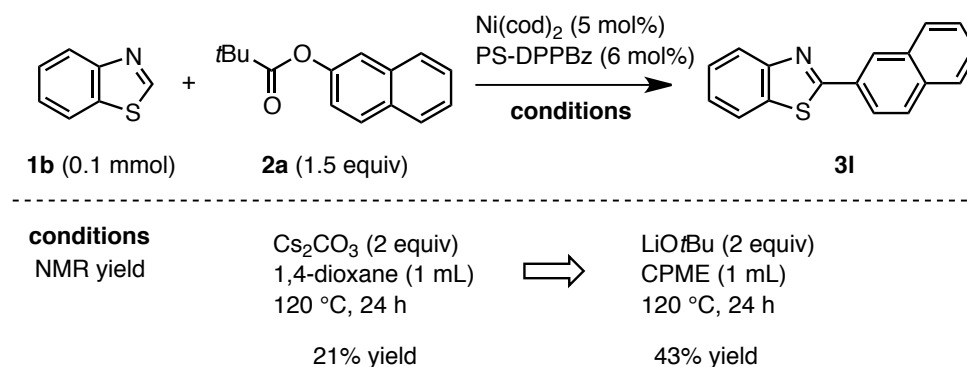
^a Conditions: **1a** (0.1 mmol), **2** (0.15 mmol), Ni(cod)₂ (5 mol% Ni), PS-DPPBz (6 mol%), Cs₂CO₃, (0.15 mmol), *m*-xylene (1 mL), 150 °C, 24 h. ^b Isolated yield. ^c Ni(cod)₂ (10 mol% Ni), PS-DPPBz (12 mol%). ^d Cs₂CO₃, (0.2 mmol). ^e In 1,4-dioxane (1 mL), at 120 °C.

Substrate Scope of azoles

Next, the author attempted the direct arylation of benzothiazoles (**1b**) with **2a** using the Ni-PS-DPPBz catalyst system under the standard conditions (with Cs₂CO₃, in 1,4-dioxane at 120 °C). However, the desired coupling product **3l** was obtained in only

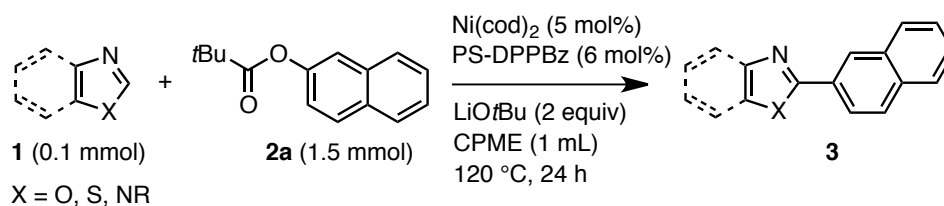
21% yield (Scheme 3). After screening the reaction conditions, the author found that the use of LiOtBu as base in CPME as solvent improved the reaction efficiency to provide **3l** in 43% yield. This catalytic performance was comparable to that of the Ni-DCYPE system (50% yield).

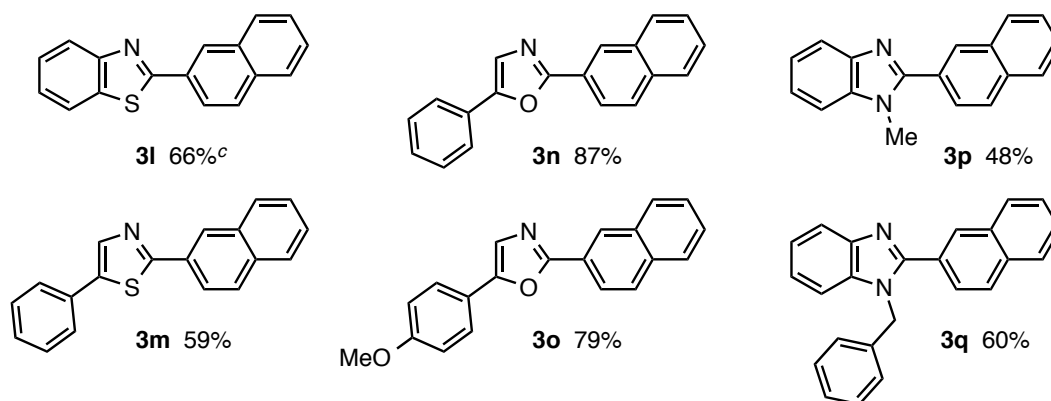
Scheme 4. Ni-catalyzed direct C–H arylation of benzothiazole (**1b**) with **2a**



The Ni-PS-DPPBz system with the modified conditions was applicable not only to thiazoles but also to oxazoles^{ref} and imidazoles. The scope of azoles is summarized in Scheme 5. For example, the reaction of 5-phenyloxazole with **2a** proceeded smoothly to produce the coupling product **3n** in high yield. Benzoimidazoles bearing methyl or benzyl substituents on the nitrogen atom afforded C2-arylated 1,3-benzoimidazoles **3n** or **3m** in acceptable yields.

Scheme 5. Ni-catalyzed C–H arylation of azoles with **2a**^{a,b}





^a Conditions: **1** (0.1 mmol), **2a** (0.15 mmol), Ni(cod)₂ (5 mol%), PS-DPPBz (6 mol%), LiOtBu, (0.2 mmol), CPME (1 mL), 120 °C, 24 h. ^b Isolated yield. ^c Ni(cod)₂ (10 mol%), PS-DPPBz (12 mol%).

Conclusion

A bisphosphine-branched phosphine PS-DPPBz enabled the Ni-catalyzed direct C–H arylation of 1,3-azoles with aryl esters, regardless of moderate electron-donating and steric natures based on a DPPBz-type ligand. The Ni-PS-DPPBz system was applicable to simple phenolic esters, for which the reported protocol with the DCYPE ligand was less effective. Various 1,3-azoles such as oxazoles, thiazoles and imidazoles participated in this Ni catalysis to provide C2-arylated azoles in moderate to high yields.

Experimental Section

Instrumentation and Chemicals

NMR spectra were recorded on a JEOL ECX-400, operating at 400 MHz for ¹H NMR, 100.5 MHz for ¹³C NMR. Chemical shift values for ¹H, ¹³C NMR spectra are referenced to Me₄Si, the residual solvent, respectively. Melting points were determined on a micro melting point apparatus using micro cover glass (Yanaco MP-500D). TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F₂₅₄. Silica gel (Kanto Chemical Co., Ltd., Silica gel 60 N, spherical, neutral) was used for column chromatography.

All reactions were carried out under nitrogen or argon atmosphere. Materials were obtained from commercial suppliers or prepared according to standard procedures

unless otherwise noted. Ni(cod)₂ was purchased from Kanto Chemical Co., Ltd., and was recrystallized from toluene/1,5-cyclooctadiene before use. Cs₂CO₃ was purchased from Junsei Chemical Co. Ltd and dried in vacuo at 120 °C, 12 h before use. LiOtBu was purchased from Aldrich Co., Ltd.. PS-TPP was prepared according to the literature¹⁰. Polystyrene supported bisphosphines were prepared from the procedure described in chapter 2 or chapter 3. All aryl pivalates^{2a}, Benzyl-1H-benzo[d]imidazole¹¹, 5-(4-methoxyphenyl)oxazole^{5a}, 5-phenyloxazole^{5a}, 5-phenylthiazole¹² were prepared according to the procedure. All solvents for catalytic reactions were degassed via three freeze–pump–thaw cycles.

Ligand Screening for Ni-catalyzed Direct C–H Arylation Between Benzoxazole (1a) and Naphthalene-2-yl Pivalate (2a) (scheme 1., entry 2)

In a glove box, ligand (0,006 mmol, 6 mol%) and anhydrous, degassed 1, 4-dioxane (0.5 mL) were placed in a 10 mL glass tube containing a magnetic stirring bar. A solution of Ni(cod)₂ (1.4 mg, 0.005 mmol, 5 mol%) in dioxane (0.5 mL) was added. After stirring 10 minutes, Cs₂CO₃ (65 mg, 0.2 mmol), naphthalene-2-yl pivalate (**2a**) (34 mg, 0.15 mmol) and benzoxazole (12 mg, 0.1 mmol) were added. The tube was sealed with a screw cap and was removed from the glove box. The mixture was stirred at 120 °C for 24 h and passed through a short silica gel pad with EtOAc. Solvent was removed under reduced pressure. An internal standard (1, 1, 2, 2-tetrachloroethane) was added to the residue. The yield of the product was determined by ¹H NMR (82%). The crude material was then purified by silica gel column chromatography (hexane/EtOAc = 9/1) to give the corresponding product **3a** (19.1 mg, 0.078 mmol in 78% isolated yield)

Ni(PS-DPPBz)-Catalyzed Direct C–H Arylation Between Benzoxazole (1a) and Various Aryl Pivalate (2) (Scheme 3)

In a glove box, PS-DPPBz (60 mg, 0,006 mmol, 6 mol%) and anhydrous, degassed *m*-xylene (0.5 mL) were placed in a 10 mL glass tube containing a magnetic stirring bar. A solution of Ni(cod)₂ (1.4 mg, 0.005 mmol, 5 mol%) in *m*-xylene (0.5 mL) was added. After stirring 10 minutes, Cs₂CO₃ (49 mg, 0.15 mmol), phenyl pivalate (**2a**) (0.15 mmol) and benzoxazole (12 mg, 0.1 mmol) were added. The tube was sealed with a screw cap and was removed from the glove box. The mixture was stirred at 150 °C for

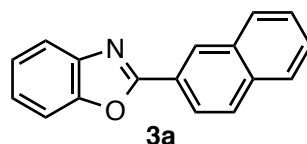
24 h and passed through a short silica gel pad with EtOAc. Solvent was removed under reduced pressure. The crude material was then purified by preparative-thin layer chromatography (hexane/EtOAc = 9/1) to give the corresponding product **3b** (16.6 mg, 0.085 mmol in 85% isolated yield)

Ni(PS-DPPBz)-Catalyzed Direct C–H Arylation Between Various Azoles and Naphthalene-2-yl Pivalate (**2a**) (Scheme 5. Synthesis of **3m**)

In a glove box, ligand (0.006 mmol, 6 mol%) and anhydrous, degassed CPME (0.5 mL) were placed in a 10 mL glass tube containing a magnetic stirring bar. A solution of Ni(cod)₂ (1.4 mg, 0.005 mmol, 5 mol%) in CPME (0.5 mL) was added. After stirring 10 minutes, LiOtBu (16 mg, 0.2 mmol), naphthalene-2-yl pivalate (**2a**) (34 mg, 0.15 mmol) and 5-phenylthiazole (0.1 mmol) were added. The tube was sealed with a screw cap and was removed from the glove box. The mixture was stirred at 120 °C for 24 h and passed through a short silica gel pad with EtOAc. Solvent was removed under reduced pressure. The crude material was then purified by silica gel column chromatography (hexane/EtOAc = 9/1) to give the corresponding product **3m** (16.9 mg, 0.059 mmol in 59% isolated yield)

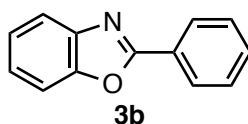
Characterization of Coupling Products

2-(Naphthalen-2-yl)benzo[d]oxazole (**3a**)



Purified by silica gel column chromatography (hexane/EtOAc = 5/95). White solid. ¹H NMR (CDCl₃) δ 7.35–7.40 (m, 2H), 7.55–7.60 (m, 2H), 7.60–7.65 (m, 1H), 7.78–7.83 (m, 1H), 7.87–7.92 (m, 1H), 7.96–8.01 (m, 2H), 8.32 (dd, *J* = 1.6 Hz, 8.4 Hz 1H), 8.79 (s, 1H). ¹³C NMR (CDCl₃) δ 110.58, 120.01, 123.94, 124.38, 124.63, 125.16, 126.89, 127.78, 127.90, 128.12, 128.76, 128.94, 132.95, 134.72, 142.21, 150.85, 163.18.

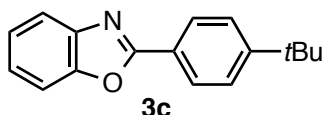
2-Phenylbenzo[d]oxazole (**3b**)



Purified by preparative thin-layer chromatography (hexane/EtOAc = 10/1). white solid.

^1H NMR (CDCl_3) δ 7.33–7.40 (m, 2H), 7.49–7.57 (m, 3H), 7.57–7.63 (m, 1H), 7.75–7.82 (m, 1H), 8.22–8.31 (m, 2H) ^{13}C NMR (CDCl_3) δ 110.58, 120.01, 124.57, 125.09, 127.15, 127.61 (2C), 128.91 (2C), 131.51, 142.09, 150.74, 163.03.

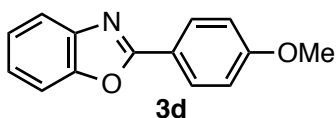
2-(4-(*tert*-Butyl)phenyl)benzo[d]oxazole (3c)



Purified by preparative thin-layer chromatography (hexane/EtOAc = 10/1). white solid.

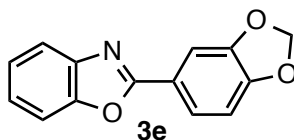
^1H NMR (CDCl_3) δ 1.38 (s, 9H), 7.25–7.36 (m, 2H), 7.52–7.61 (m, 3H), 7.74–7.80 (m, 1H), 8.19 (d, J = 8.4 Hz, 2H) ^{13}C NMR (CDCl_3) δ 31.15, 35.07, 110.51, 119.86, 124.33, 124.45, 124.85, 125.91 (2C), 127.45 (2C), 142.19, 150.70, 155.18, 163.23

2-(4-Methoxyphenyl)benzo[d]oxazole (3d)



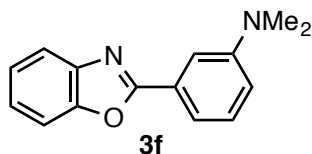
Purified by silica gel column chromatography (hexane/EtOAc = 5/1). White solid. ^1H NMR (CDCl_3) δ 3.90 (s, 3H), 7.00–7.06 (m, 2H), 7.29–7.37 (m, 2H), 7.53–7.59 (m, 1H), 7.70–7.77 (m, 1H), 8.17–8.23 (m, 2H). ^{13}C NMR (CDCl_3) δ 55.43, 110.36, 114.33 (2C), 119.59, 119.66, 124.39, 124.57, 129.35 (2C), 142.25, 150.64, 162.28, 163.15

2-(Benzo[d][1,3]dioxol-5-yl)benzo[d]oxazole (3e)



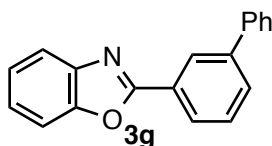
Purified by silica gel column chromatography (hexane/EtOAc = 5/1). White solid. ^1H NMR (CDCl_3) δ 6.08 (s, 2H), 6.95 (d, J = 8.4 Hz, 1H), 7.30–7.38 (m, 2H), 7.52–7.59 (m, 1H), 7.71 (d, J = 2.0 Hz, 1H), 7.72–7.77 (m, 1H), 7.83 (dd, J = 8.4, 2.0 Hz, 1H) ^{13}C NMR (CDCl_3) δ 101.74, 107.65, 108.72, 110.40, 119.69, 121.13, 122.78, 124.48, 124.76, 142.15, 148.20, 150.54, 150.64, 162.84

3-(Benzo[d]oxazol-2-yl)-*N,N*-dimethylaniline (3f)



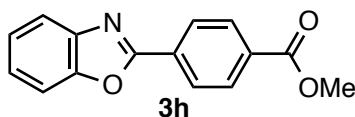
Purified by silica gel column chromatography (hexane/EtOAc = 5/1). White solid. ^1H NMR (CDCl_3) δ 3.07 (s, 6H), (dd, J = 8.0, 2.4 Hz, 1H), 7.32–7.41 (m, 3H), 7.56–7.63 (m, 3H), 7.75–7.81 (m, 1H) ^{13}C NMR (CDCl_3) δ 40.55 (2C), 110.51, 110.93, 115.52, 115.71, 119.85, 124.40, 124.85, 127.66, 129.55, 142.13, 150.67, 163.85

2-([1,1'-Biphenyl]-3-yl)benzo[d]oxazole (3g)



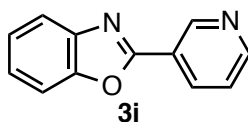
Purified by silica gel column chromatography (hexane/EtOAc = 10/1). White solid. ^1H NMR (CDCl_3) δ 7.34–7.44 (m, 3H), 7.50 (t, J = 7.2 Hz, 2H), 7.58–7.65 (m, 2H), 7.71 (d, J = 7.2 Hz, 2H), 7.76–7.84 (m, 2H), 8.25 (d, J = 8.0 Hz, 2H), 8.52 (s, 1H) ^{13}C NMR (CDCl_3) δ 110.61, 120.05, 124.63, 125.18, 126.27, 126.36, 127.22 (2C), 127.64, 127.82, 128.88 (2C), 129.39, 130.19, 140.06, 142.00, 142.08, 150.76, 162.97.

Methyl 4-(benzo[d]oxazol-2-yl)benzoate (3h)



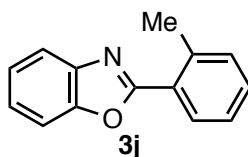
Purified by silica gel column chromatography (hexane/EtOAc = 5/1). White solid. ^1H NMR (CDCl_3) δ 3.97 (s, 3H), 7.36–7.44 (m, 2H), 7.58–7.65 (m, 1H), 7.78–7.84 (m, 1H), 8.20 (d, J = 8.4 Hz, 2H), 8.34 (d, J = 8.4 Hz, 2H). ^{13}C NMR (CDCl_3) δ 52.41, 110.76, 120.34, 124.86, 125.72, 127.48 (2C), 130.10 (2C), 131.01, 132.48, 141.98, 150.85, 161.92, 166.32

2-(Pyridin-3-yl)benzo[d]oxazole (3i)



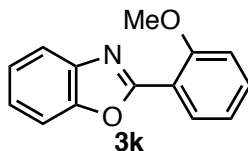
Purified by silica gel column chromatography (hexane/EtOAc = 5/1). White solid. ^1H NMR (CDCl_3) δ 7.38–7.44 (m, 2H), 7.44–7.51 (m, 1H), 7.58–7.66 (m, 1H), 7.76–7.84 (m, 1H), 8.48–8.56 (m, 1H), 8.78 (d, $J = 4.0$ Hz, 1H), 9.49 (s, 1H). ^{13}C NMR (CDCl_3) δ 110.77, 120.27, 123.52, 123.68, 124.90, 125.69, 134.75, 141.76, 148.79, 150.74, 152.07, 160.69.

2-(*o*-Tolyl)benzo[*d*]oxazole (3j)



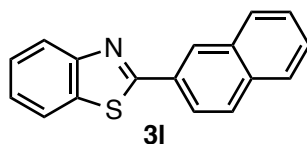
Purified by preparative thin-layer chromatography (hexane/EtOAc = 10/1). white solid. ^1H NMR (CDCl_3) δ 2.82 (s, 3H), 7.32–7.38 (m, 4H), 7.38–7.45 (m, 1H), 7.56–7.62 (m, 1H), 7.78–7.84 (m, 1H), 8.16–8.20 (m, 2H). ^{13}C NMR (CDCl_3) δ 22.2, 110.46, 120.13, 124.34, 124.99, 126.04, 129.92, 130.88, 131.77, 138.83, 142.11, 150.27, 163.38.

2-(2-Methoxyphenyl)benzo[*d*]oxazole (3k)



Purified by silica gel column chromatography (hexane/EtOAc = 5/1). White solid. ^1H NMR (CDCl_3) δ 4.03 (s, 3H), 7.08–7.15 (m, 2H), 7.31–7.38 (m, 2H), 7.52 (td, $J = 8.0$, 1.6 Hz), 7.57–7.62 (m, 1H), 7.79–7.86 (m, 1H), 8.15 (dd, $J = 8.0$, 1.6 Hz). ^{13}C NMR (CDCl_3) δ 56.21, 110.42, 112.03, 116.16, 120.23, 120.70, 124.23, 124.90, 131.28, 132.74, 142.14, 150.30, 158.44, 161.52.

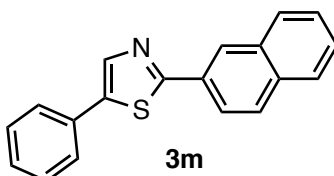
2-(Naphthalen-2-yl)benzo[*d*]thiazole (3l)



Purified by preparative thin-layer chromatography (hexane/EtOAc = 5/1). white solid. ^1H NMR (CDCl_3) δ 7.37 (t, $J = 7.2$ Hz, 1H), 7.48 (t, $J = 8.4$ Hz, 2H), 7.50 (s, 1H), 7.52–7.58 (m, 2H), 7.78 (d, $J = 7.2$ Hz, 2H), 7.84–7.91 (m, 1H), 7.91–8.00 (m, 2H),

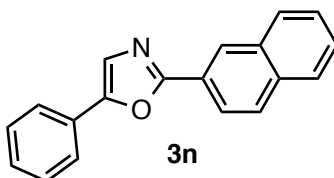
8.20 (dd, $J = 8.4, 1.6$ Hz, 1H), 8.61 (s, 1H). ^{13}C NMR (CDCl_3) δ 123.27, 123.64, 124.25, 124.73, 126.12, 126.79, 127.25, 127.89, 128.02, 128.50, 128.69, 128.96, 133.08, 134.13, 151.45, 161.32

2-(Naphthalen-2-yl)-5-phenylthiazole (3m)



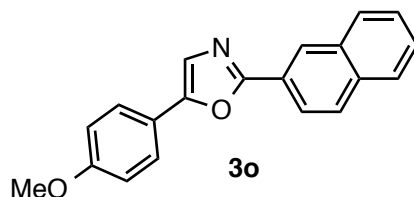
Purified by silica gel column chromatography (hexane/EtOAc = 5/1). White solid. ^1H NMR (CDCl_3) δ 7.35 (t, $J = 7.2$ Hz, 1H), 7.43 (t, $J = 7.2$ Hz, 2H), 7.48–7.757 (m, 2H), 7.64 (d, $J = 7.2$ Hz, 2H), 7.82–7.88 (m, 1H), 7.88–7.96 (m, 2H), 8.05–8.11 (m, 2H), 8.45 (s, 1H). ^{13}C NMR (CDCl_3) δ 123.76, 125.77, 126.66 (2C), 126.79, 127.00, 127.83, 128.33, 128.60, 128.76, 129.13 (2C), 130.99, 131.38, 133.24, 134.06, 139.29, 139.40

2-(Naphthalen-2-yl)-5-phenyloxazole (3n)



Purified by preparative thin-layer chromatography (hexane/EtOAc = 5/1). white solid. ^1H NMR (CDCl_3) δ 7.36–7.43 (m, 1H), 7.47–7.58 (m, 3H), 7.83–7.90 (m, 1H), 7.90–8.00 (m, 3H), 8.11 (d, $J = 8.4$ Hz, 1H), 8.21 (dd, $J = 8.4$ Hz, 2.0 Hz), 8.56 (s, 1H). ^{13}C NMR (CDCl_3) δ 121.63 (2C), 123.21, 124.42, 125.21, 126.86, 127.43, 127.51, 127.59, 127.85 (2C), 128.80, 130.95, 133.15, 134.57, 135.09, 154.20, 168.08

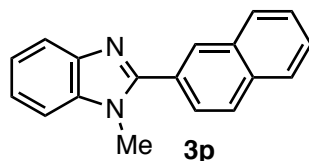
5-(4-Methoxyphenyl)-2-(naphthalen-2-yl)oxazole (3o)



Purified by preparative thin-layer chromatography (hexane/EtOAc = 4/1). Pale yellow

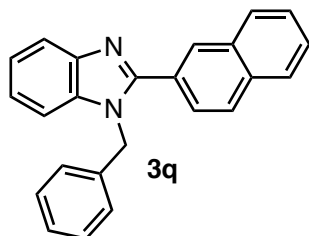
solid. ^1H NMR (CDCl_3) δ 3.87 (s, 3H), 6.97–7.03 (m, 2H), 7.38 (s, 1H), 7.50–7.57 (m, 2H), 7.68–7.74 (m, 2H), 7.84–7.90 (m, 1H), 7.91–8.00 (m, 2H), 8.18 (dd, J = 8.4, 1.6 Hz), 8.58 (s, 1H) ^{13}C NMR (CDCl_3) δ 55.35, 114.39 (2C), 120.84, 122.12, 123.21, 124.83, 125.77 (2C), 125.83, 126.71, 127.10, 127.85, 128.60, 128.63, 133.07, 133.99, 151.47, 159.82, 160.69

1-Methyl-2-(naphthalen-2-yl)-1H-benzo[d]imidazole (3p)



Purified by silica gel column chromatography (hexane/EtOAc = 1/1). White solid. ^1H NMR (CDCl_3) δ 3.96 (s, 3H), 7.31–7.39 (m, 2H), 7.41–7.47 (m, 1H), 7.54–7.62 (m, 2H), 7.84–8.03 (m, 5H), 8.27 (s, 1H) ^{13}C NMR (CDCl_3) δ 31.85, 109.62, 119.87, 122.49, 122.82, 126.32, 126.75, 127.20, 127.52, 127.82, 128.45, 128.50, 129.33, 132.92, 133.58

1-Benzyl-2-(naphthalen-2-yl)-1H-benzo[d]imidazole (3q)



Purified by silica gel column chromatography (hexane/EtOAc = 1/1). White solid. ^1H NMR (CDCl_3) δ 5.53 (s, 2H), 7.17 (d, J = 7.2 Hz, 2H), 7.26–7.30 (m, 2H), 7.31–7.40 (m, 4H), 7.53 (quint-d, J = 7.2, 1.2 Hz, 2H), 7.76–7.84 (m, 2H), 7.86–7.95 (m, 3H), 8.16 (s, 1H) ^{13}C NMR (CDCl_3) δ 48.54, 122.74, 123.12, 126.01 (2C), 126.13, 126.68, 127.20, 127.31, 127.75, 127.82, 128.53 (2C), 129.09 (2C), 129.22, 132.86, 133.67, 136.51, 143.25, 154.15

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- (9) Benzoxazole was not applicable in the conditions.
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Publication List

- Chapter 1** “Threefold Cross-Linked Polystyrene–Triphenylphosphane Hybrids: Mono-P-Ligating Behavior and Catalytic Applications for Aryl Chloride Cross-Coupling and C(sp³)–H Borylation”
Tomohiro Iwai, Tomoya Harada, Kenji Hara and Masaya Sawamura
Angew. Chem. Int. Ed. **2013**, 52, 12322–12326.

Other publications not included in this thesis.

- (1) “Intramolecular Hydroamination of Alkynic Sulfonamides Catalyzed by Gold-Triethynylphosphine Complex: Construction of Azepine Frameworks by 7-Exo-dig Cyclization”
Hideto Ito, Tomoya Harada, Hirohisa Ohmiya, Masaya Sawamura
Beilstein. J. Org. Chem. **2011**, 7, 951–959.
- (2) “Tripod Immobilization of Triphenylphosphane on a Silica Gel Surface to Enable Selective Mono-P-ligation to Palladium: Application to Suzuki–Miyaura Cross-Coupling with Chloroarenes”.
Tomohiro Iwai, Ryotaro Tanaka, Tomoya Harada, Masaya Sawamura
Chem. Eur. J. **2014**, 20, 1057–1065.
- (3) “Silica-supported Tripod Triarylphosphines: Application to Palladium Catalyzed Borylation of Chloroarenes”.
Tomohiro Iwai, Tomoya Harada, Ryotaro Tanaka, Masaya Sawamura
Chem. Lett. **2014**, 43, 584–586.
- (4) “Silica-Supported Tripod Triarylphosphane: Application to Transition Metal Catalyzed C(sp³)–H Borylations”.
Tomohiro Iwai, Ryo Murakami, Tomoya Harada, Soichiro Kawamorita, Masaya Sawamura
Adv. Synth. Catal. **2014**, 356, 1563–1570.

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