

Development of Efficient and Reusable Diarylphosphinopolystyrene-Supported Palladium Catalysts for C–C Bond Forming Cross-Coupling Reactions

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Abstract: Short and versatile syntheses of reusable diarylphosphinopolystyrene-supported palladium catalysts **3a–j** are described. The bis(*o*-tolyl)phosphino catalyst **3b** is particularly efficient for the Suzuki and Sonogashira cross-couplings, whereas the bis(*m*-tolyl)phosphino catalyst **3c** is the most active catalyst for Heck reactions. The couplings are performed under non-anhydrous reaction conditions and require only low amounts of supported palladium (0.5

mequivs. for Suzuki–Miyaura, 1.0 mequiv. for Sonogashira and 0.5 mequivs. for Heck reactions could be sufficient). Catalysts **3a–j** are recovered by filtration and can be reused more than four times with no loss of efficiency.

Keywords: C–C coupling; heterogeneous catalysis; palladium; phosphane ligands; polymers

Introduction

The formation of new aryl–aryl, aryl–alkynyl or aryl–alkenyl bonds in a single step by transition metal-catalyzed cross-coupling reactions is a fundamental transformation in modern organic synthesis.^[1] Among palladium-catalyzed couplings, the Suzuki–Miyaura,^[1a,2] Sonogashira^[3] and Heck^[4] reactions are the most widely used. They find widespread applications, especially for the preparation of molecules possessing interesting biological^[5] or physical^[6,7] properties and are often performed on a very large scale.^[8]

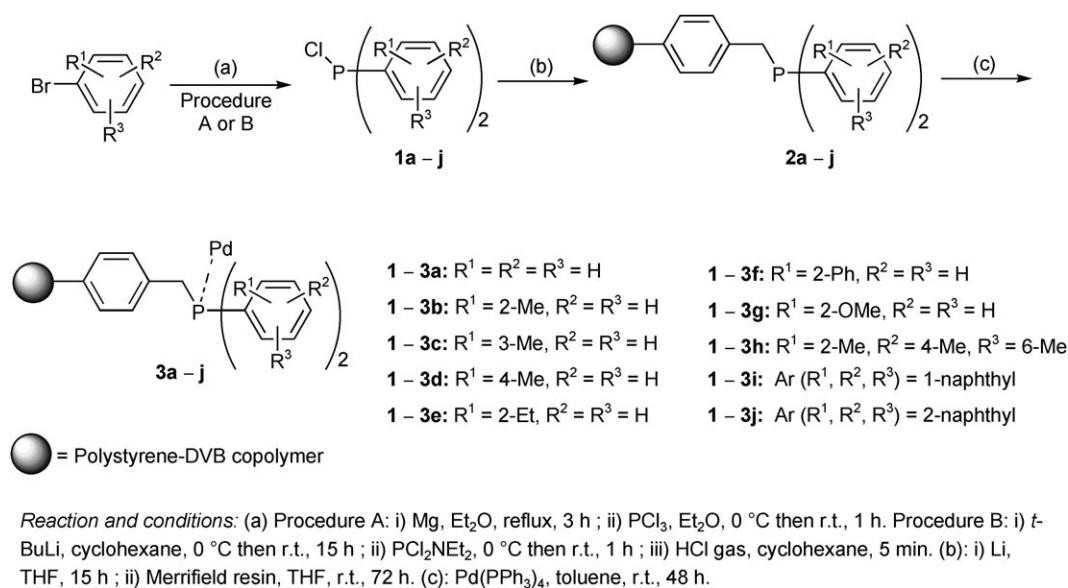
These cross-coupling reactions generally proceed in high yields under mild and non-anhydrous reaction conditions and tolerate the presence of many functional groups. They are usually carried out in the presence of a soluble (i.e., homogeneous) palladium catalyst. During the last decade, considerable work has been devoted to the development of homogeneous catalysts.^[1] However, their major drawbacks are the impossibility to recover, for direct reuse, these expensive catalysts and the difficulties frequently encountered to avoid the presence of the transition metal in the reaction products. Therefore, recoverable and reusable heterogeneous palladium catalysts, able to replace their homogeneous counterparts for C–C bond forming reactions, have been recently developed.^[9]

The metal is generally grafted on inorganic^[10] or organic supports, especially on polymers.^[11–14] For example, palladium can be encapsulated or incarcerated^[11,12] in a polymeric matrix or anchored on polymer-supported phosphines^[13a–l] or carbenes.^[13n–p] An important environment-related preoccupation is to minimize the amount of palladium required for these cross-coupling reactions. We present here polystyrene-supported catalysts which are very active (only low amounts of supported palladium are required), versatile and easy to prepare from usual Merrifield polymers.^[14]

Results and Discussion

Preparation of Diarylphosphinopolystyrene-Supported Palladium Catalysts **3a–j**

The syntheses of catalysts **3a–j** were performed in two steps: nucleophilic substitution of the chlorine atoms of a Merrifield resin by diarylphosphinolium (Ar_2PLi) followed by introduction of palladium with a soluble palladium source (Scheme 1). The required diarylphosphinolium reagents were generated from the corresponding diarylchlorophosphines **1a–j** using a metal/halogen exchange reaction.



Scheme 1. Preparation of diarylphosphinopolystyrene-supported palladium catalysts **3a–j**.

The usual method to prepare the diarylchlorophosphines **1b–j** consists of the reaction of a Grignard reagent with PCl₃ (Scheme 1, procedure A).^[15] This methodology was only practicable for the preparation of **1b** and **1h**. The syntheses of **1c–g** and **1i** and **j** using this method were in most instances either unsuccessful or tedious despite optimization attempts. By reacting aryllithium reagents with PCl₂NEt₂ followed by acidification of the reaction mixture with anhydrous HCl^[16] (Scheme 1, procedure B), diarylchlorophosphines **1c–g**, and **1i** and **j** were obtained with over 90 % purity (determined by ¹H and ³¹P NMR of the crude mixtures). Interestingly, the reaction of arylmagnesium bromides with PCl₂NEt₂ failed and only degradation products could be observed.

Because of their sensitivity to air and moisture, the crude diarylchlorophosphines **1a–j** were directly reacted with lithium in THF at room temperature. The resulting dark red solutions were transferred to suspensions of a Merrifield resin in THF to afford diarylphosphinopolystyrenes **2a–j**. As indicated by P and Cl elemental analysis, in most cases, *ca.* 70 % of the chlorine atoms of the resin were replaced by Ar₂P groups, and only *ca.* 1 % of chlorine atoms remained.

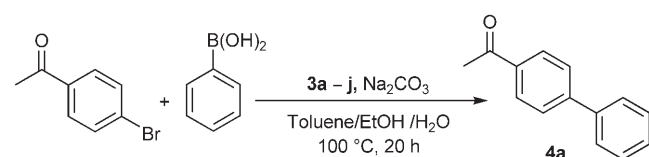
Polystyrene-supported palladium catalysts **3a–j** were prepared using an exchange reaction with Pd(PPh₃)₄ (as a soluble palladium source) in toluene at room temperature (Scheme 1). In each case, 4 equivs. of PPh₃ were recovered.^[14a] Elemental analysis showed that more than 95 % of the amount of palladium present was grafted to the polystyrene supports **2a–j**. These syntheses can be efficiently performed on a large scale (*ca.* 50 g). Comparable P/Pd ratios were

therefore obtained for **3a–h** (for further details see Supporting Information). All the catalysts are air- and moisture-stable and can therefore be easily stored.

Suzuki–Miyaura Cross-Coupling Reactions of Aryl Bromides and Boronic Acids with Catalysts **3a–j**

The activities of catalysts **3a–j** were evaluated for Suzuki–Miyaura cross-coupling reactions using as model substrates 4-bromoacetophenone and phenylboronic acid (Table 1).

Replacement of the phenyl groups on the phosphorus atom by *o*-tolyl groups brought about a significant improvement: **4a** could be quantitatively obtained with only 0.5 mequivs. of polystyrene-supported palladium catalyst **3b** (entries 1 and 2). Catalyst **3b'** (prepared, as **3b**, from phosphinated resin **2b** but containing 0.6 % of palladium) afforded also a quantitative transformation when 0.5 mequivs. of supported palladium were used. In the presence of only 0.05 mequivs. of polystyrene-supported palladium catalyst **3b**, a lower but still high 86 % yield was obtained (entry 3). Moderate yields were observed at lower temperatures or with shorter reaction times. The nature of the aryl groups on the phosphorus atom is of crucial importance: *o*-tolyl, 2-ethylphenyl and 2-biphenyl groups afforded the best catalysts (entries 3, 6 and 7). Lower yields were obtained with catalysts **3c** and **d** and **3g–j** (entries 4, 5 and 8–11). It should be noted, however, that all catalysts have an excellent activity: in the presence of 0.5 mequivs. of polystyrene-supported palladium, almost quantitative yields of **4a** were ob-

Table 1. Suzuki–Miyaura couplings of 4-bromoacetophenone and phenylboronic acid using **3a–j**.

Entry ^[a]	Catalyst ^[b]	Pd [mequiv(s.)]	Calculated Yields [%] ^[c]
1	3a	0.5	77
2	3b	0.5	100
3	3b	0.05	86
4	3c	0.05	25
5	3d	0.05	< 10
6	3e	0.05	82
7	3f	0.05	74
8	3g	0.05	31
9	3h	0.05	< 10
10	3i	0.05	15
11	3j	0.05	28
12	Pd EnCat TPP30	1.0	31
13	Pd EnCat NP30	1.0	12

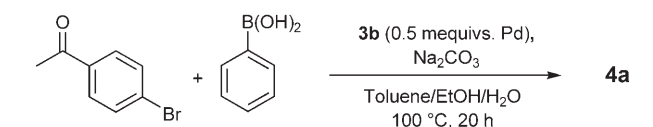
^[a] Reactions performed with 1.0 equiv. of 4-bromoacetophenone, 1.1 equivs. of phenylboronic acid, 1.2 equivs. of Na₂CO₃ and the amount of catalyst containing the indicated number of Pd mequivs. in a 5:1:1 mixture of toluene/EtOH/H₂O.

^[b] Catalysts **3a–j** contain 0.3 % of palladium.

^[c] Yields were calculated by ¹H NMR of the crude reaction mixtures.

tained with all catalysts except **3a**, **3d** and **3h**. In addition, the Suzuki–Miyaura reaction can be carried out successfully without an argon atmosphere. The amount of palladium leached in the reaction medium was then determined after complete mineralization of the filtrate obtained at the end of the reaction (entry 2, for further details see Experimental Section and Supporting Information). We found that less than 1 % of the initial amount of supported palladium was leached during the Suzuki–Miyaura coupling. This result is in accordance with previous literature reports.^[17] A hot filtration test was then performed. For this purpose, after 1 h of reaction (yield of **4a** at that point: 30 %), **3b** was filtered and the filtrate was heated at 100 °C for another 19 h after which the yield attained only 42 %.

In a similar experiment the yields were 8 % (after *ca.* 40 min) and only 10 % after hot filtration and further 20 h at 100 °C. Additionally, the amount of palladium present in the filtrate obtained by hot filtration was found to be only 0.9–1.2 % of the initial amount.

Table 2. Recycling test of **3b** for Suzuki–Miyaura cross-coupling reaction.

Run ^[a,b]	1	2	3	4
Calculated Yields [%] ^[c]	100	100	100	96

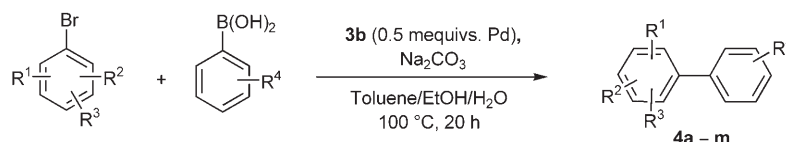
^[a] Reactions performed with 1.0 equiv. of 4-bromoacetophenone, 1.1 equivs. of phenylboronic acid, 1.2 equivs. of Na₂CO₃ in a 5:1:1 mixture of toluene/EtOH/H₂O.

^[b] Catalyst **3b** contains 0.3 % of palladium.

^[c] Yields were calculated by ¹H NMR of the crude reaction mixtures.

Therefore, the soluble catalytic entities played no significant role for this coupling. Unfortunately, the reaction of 4-chloroacetophenone with phenylboronic acid, even in the presence of 20 mequivs. of polystyrene-supported palladium catalyst **3b**, proceeded with a low 19 % yield and optimization attempts (nature of the base, of the solvent or presence of microwave irradiation) were unsuccessful. The activity of **3b** was similar to that of the soluble palladium Pd(PPh₃)₄ catalyst [quantitative yield of **4a** in the presence of 0.5 mequivs. of Pd(PPh₃)₄]. However, it is interesting to note that the activity of **3b** was significantly superior to that of the commercially available heterogeneous palladium encapsulated catalysts Pd EnCat TPP30 and Pd EnCat NP30, which afforded **4a** with, respectively, 31 % and 12 % yields even in the presence of 1.0 mequiv. of supported palladium (entries 12 and 13). This was not unexpected since literature reports mentioned the use of 50 mequivs. of polymer encapsulated palladium.^[11a] Similar results have also been described with palladium incarcerated catalysts.^[12d] To ascertain the possibilities of reuse, **3b** was recovered by filtration, washed and reintroduced in a coupling reaction. This sequence was run four times with no significant decrease in yield (Table 2).

Various aryl bromides and arylboronic acids were cross-coupled in the presence of **3b** under our optimized reaction conditions (Table 3). The couplings of 4-bromoacetophenone with electron-deficient or electron-rich arylboronic acids afforded the desired biaryls **4a–d** in > 90 % isolated yields (entries 1–4). Excellent results were also obtained by reacting phenylboronic acid with both activated or deactivated aryl bromides to afford the expected products **4e–l** (entries 5–12). Interestingly, the reaction of the sterically hindered bromomesitylene with phenylboronic acid furnished **4m** in a high 93 % isolated yield (entry 13). In addition, cross-couplings of phenylboronic acid with

Table 3. Suzuki–Miyaura cross-couplings of various aryl bromides and arylboronic acids using **3b**.

Entry ^[a,b]	R ¹	R ²	R ³	R ⁴	Product	Isolated Yields [%] ^[c]
1	4-Ac	H	H	H	4a	98
2	4-Ac	H	H	3-NO ₂	4b	92
3	4-Ac	H	H	2-Me	4c	90
4	4-Ac	H	H	4-OMe	4d	97
5	3-Ac	H	H	H	4e	98
6	2-Ac	H	H	H	4f	97
7	4-NO ₂	H	H	H	4g	77
8	H	H	H	H	4h	87
9	4-Me	H	H	H	4i	91
10	3-Me	H	H	H	4j	96
11	2-Me	H	H	H	4k	92
12	4-NH ₂	H	H	H	4l	94
13	2-Me	4-Me	6-Me	H	4m	56 (93) ^[d]

^[a] Reactions performed with 1.0 equiv. of 4-bromoacetophenone, 1.1 equivs. of phenylboronic acid, 1.2 equivs. of Na₂CO₃ in a 5:1:1 mixture of toluene/EtOH/H₂O.

^[b] Catalyst **3b** contains 0.3 % of palladium.

^[c] Isolated yields after filtration of the crude reaction mixture on silica gel.

^[d] Isolated yield in the presence of 5.0 mequivs. of supported palladium.

4-bromopyridine and (*E*)-1-bromo-2-phenylethylene yielded quantitatively the expected products.

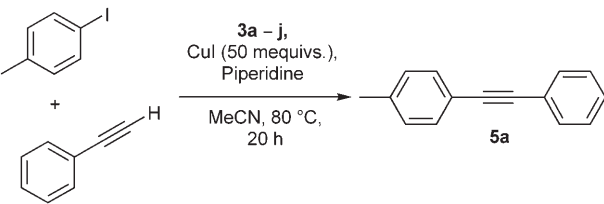
Sonogashira Cross-Coupling Reactions of Aryl Iodides and Alkynes with Catalysts **3a–j**

The activities of catalysts **3a–j** were then evaluated for Sonogashira cross-coupling reactions: 4-iodotoluene and phenylacetylene were used as model substrates (Table 4).

Catalysts **3a** and **3b** were the most efficient for the Sonogashira coupling and the desired alkyne **5a** was obtained in almost quantitative yield (entries 1–3). In the presence of only 1.0 mequiv. of supported palladium a still quantitative yield was observed using **3b** (entry 3). A hot filtration test was then performed with **3b** (entry 3, but with 2.5 mequivs. of supported palladium). For this purpose, **3b** was filtered after 10 min of reaction (yield of **5a** at that point: 52 %) and the filtrate was heated at 80 °C for another 12 h after which only an 82 % yield was obtained. Additionally, mineralization of this filtrate showed that 1.7 % of the initial amount of palladium was present in the reaction medium. The amount of palladium leached was also determined at the end of the reaction and found to be 1–2 % of the initial amount. Hence, the soluble catalytic entities somehow played a role. In the presence of only 0.5 mequivs. of supported palladium (**3b**) the yield dropped to 31 %. In

the absence of CuI or at lower temperatures, the coupling of 4-bromotoluene and phenylacetylene did not afford the expected alkyne in reasonable yield even in the presence of larger amounts of supported palladium and complex reaction mixtures, including probably homocoupling products, were obtained. Lower yields were observed using catalysts bearing di(*m*- or *p*-tolyl)phosphino groups or several di(*ortho*-substituted phenyl)phosphino groups (entries 4–8). The sterically more hindered **3h–j** afforded only complex reaction mixtures (entries 9–11). For comparison purposes, the reaction was run with 1.0 mequiv. of the soluble Pd(PPh₃)₄ catalyst: **5a** was quantitatively formed. The efficiencies of heterogeneous catalysts Pd EnCat TPP30 and Pd EnCat NP30 were then compared to that of **3b**. Alkyne **5a** was obtained, respectively, only in 85 % and 40 % yields even in the presence of 2.5 mequivs. of supported palladium (entries 12 and 13). Noteworthy, the use of heterogeneous palladium catalysts for Sonogashira reactions has been only sparsely described.^[18] A recycling test of **3b** showed that this catalyst can be reused at least four times (Table 5).

The Sonogashira reaction was then run on various aryl iodides and alkynes (Table 6). It turned out that in the presence of 2.5 mequivs. of polystyrene-supported palladium, only moderate yields (*ca.* 80 %) were obtained in most cases. Therefore 5.0 mequivs. of polystyrene-supported palladium were used for these couplings. The desired coupling products **5a–g** were obtained for both electron-rich and electron-de-

Table 4. Sonogashira couplings of 4-iodotoluene and phenylacetylene using **3a–j**.


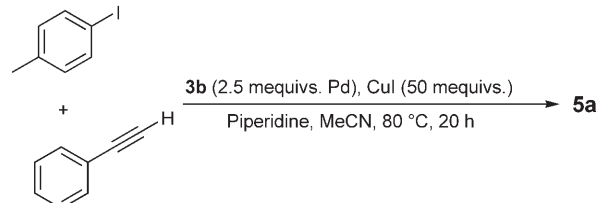
Entry ^[a]	Catalyst ^[b]	Pd [mequiv(s).]	Calculated Yields [%] ^[c]
1	3a	2.5	100
2	3a	1.0	98
3	3b	1.0	100
4	3c	1.0	80
5	3d	1.0	77
6	3e	1.0	81
7	3f	1.0	92
8	3g	1.0	74
9	3h	1.0	< 20 ^[d]
10	3i	1.0	< 20 ^[d]
11	3j	1.0	< 20 ^[d]
12	Pd EnCat TPP30	2.5	85
13	Pd EnCat NP30	2.5	40

^[a] Reactions performed with 1.0 equiv. of 4-iodotoluene, 1.2 equivs. of phenylacetylene, 1.2 equivs. of piperidine, 50 mequivs. of CuI and the amount of catalyst containing the indicated number of Pd mequivs.

^[b] Catalysts **3a–j** contain 0.3 % of palladium.

^[c] Yields were calculated by ¹H NMR of the crude reaction mixtures.

^[d] Complex reaction mixtures were obtained.

Table 5. Recycling test of catalyst **3b** for Sonogashira cross-coupling reaction.


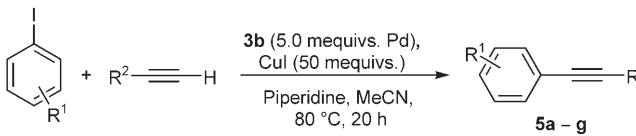
Run ^[a,b]	1	2	3	4
Calculated Yields [%] ^[c]	100	100	94	95

^[a] Reactions performed with 1.0 equiv. of 4-iodotoluene, 1.2 equivs. of phenylacetylene, 1.2 equivs. of piperidine.

^[b] Catalyst **3b** contains 0.3 % of palladium.

^[c] Yields are calculated by ¹H NMR of the crude reaction mixtures.

efficient aryl iodides with excellent isolated yields (entries 1–6). The sterically more hindered 1-bromo-2-iodobenzene also gave the desired alkyne in 91 % yield

Table 6. Sonogashira cross-couplings of various aryl iodides and alkynes using **3b**.


Entry ^[a,b]	R ¹	R ²	Product	Isolated Yields [%] ^[c]
1	4-Me	Ph	5a	98
2	3-Me	Ph	5b	92
3	2-Br	Ph	5c	91
4	4-OMe	Ph	5d	83
5	H	Ph	5e	99
6	4-Ac	Ph	5f	91
7	4-Me	CH ₂ OH	5g	78

^[a] Reactions performed with 1.0 equiv. of aryl iodide, 1.2 equivs. of alkyne, 1.2 equivs. of piperidine.

^[b] Catalyst **3b** contains 0.3 % of palladium.

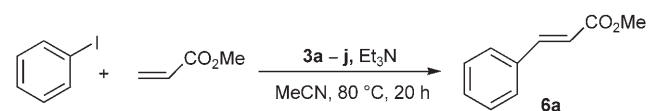
^[c] Isolated yields after filtration of the crude reaction mixture on silica gel.

(entry 3). By using 4-iodotoluene and propargylic alcohol a somewhat lower yield of 78 % was observed (entry 7). Sonogashira couplings were also successfully performed between phenylacetylene and 1-iodonaphthalene or 2-iodothiophene, with only 2.5 mequivs. of supported palladium (isolated 96 % and 98 % yields, respectively). It should be noted that, contrary to the Suzuki–Miyaura reaction, an argon atmosphere is required for this coupling.

Heck Cross-Coupling Reactions of Aryl Iodides and Alkenes with Catalysts **3a–j**

The synthetic potential of catalysts **3a–j** was then evaluated for the Heck reaction: iodobenzene and methyl acrylate were chosen as model substrates (Table 7).

Catalyst **3a** afforded the desired alkene **6a** with almost quantitative yields in the presence of 2.5 or 1.5 mequivs. of polystyrene-supported palladium (entries 1 and 2). Surprisingly, **3b** afforded **6a** with a very low yield of 8 % (entry 3). A much improved catalytic activity was obtained by replacing the diphenylphosphino groups by di(*m*-tolyl)phosphino groups: **6a** was quantitatively obtained with only 1.5 or 0.5 mequivs. of polystyrene-supported palladium catalyst **3c** (entries 4 and 5). At lower temperatures or in the presence of < 0.5 mequivs. of supported palladium, quantitative yields could not be achieved even with the very efficient catalyst **3c**. The coupling of bromobenzene with methyl acrylate gave no **6a** even in the presence of 10 mequivs. of polystyrene-supported palladium and optimization attempts (nature of the base, of the solvent or presence of various phosphine addi-

Table 7. Heck couplings of iodobenzene and methyl acrylate using **3a–j**.

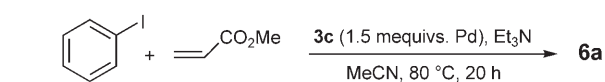
Entry ^[a]	Catalyst ^[b]	Pd [mequivs.]	Calculated Yields [%] ^[c]
1	3a	2.5	99
2	3a	1.5	96
3	3b	1.5	8
4	3c	1.5	100
5	3c	0.5	100
6	3d	1.5	95
7	3e	1.5	98
8	3f	1.5	97
9	3g	1.5	98
10	3h	1.5	17
11	3i	1.5	87
12	3j	1.5	97
13	Pd EnCat TPP30	0.5	57
14	Pd EnCat NP30	0.5	100

^[a] Reactions performed with 1.0 equiv. of iodobenzene, 2.0 equivs. of methyl acrylate, 1.2 equivs. of Et₃N and the amount of catalyst containing the indicated number of Pd mequivs.

^[b] Catalysts **3a–j** contain 0.3 % of palladium.

^[c] Yields were calculated by ¹H NMR of the crude reaction mixtures.

tives) were unsuccessful. With catalysts bearing di(*p*-tolyl)phosphino groups or several di(*ortho*-substituted phenyl)phosphino groups, **6a** was obtained with excellent yields (entries 6–9). No further improvement was observed with the sterically more hindered catalysts **3h–j** (entries 10–12). Remarkably, the Heck reaction can be performed successfully without an argon atmosphere. A hot filtration test was then carried out. After 30 min of reaction at 80 °C (entry 4), **3c** was removed by filtration (yield of **6a** at this point: 9 %) and the filtrate was heated at 80 °C for another 20 h after which a significantly better yield of 70 % was obtained. We determined, after total mineralization of the filtrate obtained by hot filtration, that the amount of palladium present in the filtrate was very dependent on the progress of the reaction: 11 % of the initial amount were present after 30 min, 30 % after 1 h and only 2.5 % after 4 h. Therefore soluble palladium entities participate in the Heck cross-coupling reaction. After the normal end of the reaction (entry 4), the amount of palladium found in the filtrate and on the walls of the reaction vessel was 1–2.5 % of the initial amount. These results prove that a redeposition of the metal on the catalyst itself occurred^[19] and it should furthermore be noted that TEM images of the

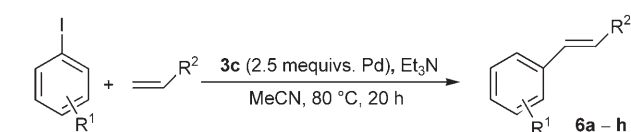
Table 8. Recycling test of catalyst **3c** for Heck cross-coupling reaction.

Run ^[a,b]	1	2	3	4
Calculated Yields [%] ^[b]	100	98	100	97

^[a] Reactions performed with 1.0 equiv. of iodobenzene, 2.0 equivs. of methyl acrylate and 1.2 equivs. of Et₃N.

^[b] Catalyst **3c** contains 0.3 % of palladium.

^[c] Yields were calculated by ¹H NMR of the crude reaction mixtures.

Table 9. Heck cross-couplings of various aryl iodides and alkenes with **3c**.

Entry ^[a,b]	R ¹	R ²	Product	Isolated Yields [%] ^[c]
1	H	CO ₂ Me	6a	98
2	4-Me	CO ₂ Me	6b	94
3	3-Me	CO ₂ Me	6c	98
4	2-Br	CO ₂ Me	6d	85
5	4-OMe	CO ₂ Me	6e	98
6	3-CF ₃	CO ₂ Me	6f	96
7	4-Ac	CO ₂ Me	6g	80
8	H	Ph	6h	98

^[a] Reactions performed with 1.0 equiv. of aryl iodide, 2.0 equivs. of alkene, 1.2 equivs. of Et₃N.

^[b] Catalyst **3c** contains 0.3 % of palladium.

^[c] Isolated yields after filtration of the crude reaction mixture on silica gel.

new catalyst and of the recovered catalyst are very similar (for an example, see Supporting Information). In addition, in each case only the (*E*)-alkene **6a** was formed. In the presence of the homogeneous Pd(PPh₃)₄ catalyst (1.5 mequivs.), **6a** was quantitatively obtained. The activity of catalyst **3c** was then compared to those of the heterogeneous catalysts Pd EnCat TPP30 and Pd EnCat NP30. Under the optimized reaction conditions, Pd EnCat TPP30 afforded **6a** in only 57 % yield in the presence of 0.5 mequivs. of encapsulated palladium, whereas a quantitative yield was observed with Pd EnCat NP30 (entries 13 and 14). Polymer-incarcerated palladium catalysts were reported to afford the desired products in high yields but in the presence of 50 mequivs. of palladium.^[12d] Other polymer-supported N-heterocyclic carbene-based palladium catalysts have been reported for Heck couplings of aryl iodides and alkenes using 10 mequivs. of palladium.^[13p] Catalyst **3c** appears

therefore to be very efficient, and moreover a recycling test showed that it can be reused at least four times (Table 8).

The scope of the Heck reaction was then evaluated with various aryl iodides and alkenes in the presence of 2.5 mequivs. of supported palladium using **3c** (Table 9). Electron-rich or electron-deficient aryl iodides were efficiently cross-coupled with methyl acrylate to afford alkenes **6a–g** with excellent isolated yields (entries 1–7). Noteworthy, the sterically hindered 1-bromo-2-iodobenzene gave **6d** in a good 85 % yield (entry 4). The coupling of iodobenzene and styrene afforded the desired product **6h** in 98 % isolated yield (entry 8). Cross-couplings of methyl acrylate with 2-iodothiophene or 1-iodonaphthalene were also performed in, respectively, 91 % and 98 % isolated yields. In all cases only the (*E*)-alkenes were observed.

Conclusions

In conclusion, short and efficient syntheses of air- and moisture-stable, easy to recover and reuse, diarylphosphinopolystyrene-supported palladium catalysts have been developed. They can successfully be used for crucial C–C bond forming cross-coupling reactions under non-anhydrous reaction conditions in the presence of low amounts of supported palladium. Our catalysts are clearly more active than the commercially available heterogeneous catalysts Pd EnCat. Several batches of catalysts **3b** and **3c** were studied by transmission electron microscopy (TEM, see Supporting Informations). It was found that some catalysts showed many palladium crystallites whereas these were very scarce on other batches of the same catalysts. The palladium crystallites had a diameter of up to *ca.* 10 nm. It should be noted that the yields obtained in the coupling reactions were constant from catalyst batch to catalyst batch and therefore not related to the abundance of crystallites. No structural modification of a catalyst after use could be shown by TEM, even for the Heck reaction where redeposition of the metal was proven by elemental analysis. This suggests that the “soluble” catalytic entities of the reaction are palladium complexes and not nanoparticles.

Experimental Section

General Remarks

The reagents were obtained from commercial sources and were used without further purifications. THF, Et₂O and cyclohexane were distilled from sodium/benzophenone. The syntheses of compounds **1b** and **c**, resins **2b** and **c** and cata-

lysts **3b** and **c** were carried out in anhydrous glassware under an atmosphere of argon. The diarylchlorophosphines were stored in dry glassware under an atmosphere of argon. PCl₂NEt₂ was prepared according to literature reports.^[16] The Merrifield resin was purchased from Polymer Laboratories (PL-CMS Resin, 0.86 mmol g^{−1}, 75–150 μm). The reaction mixtures were filtered on a Schleicher & Schuell polytetrafluoroethylene membrane filter (0.2 μm). Purifications of compounds **4a–m**, **5a–g**, **6a–h** were performed by filtration on silica gel (40–63 μm, Merck). ¹H and ³¹P NMR spectra were recorded using a 400 MHz instrument in CDCl₃. Chemical shifts are reported in parts per million (δ) downfield from TMS. Spin multiplicities are indicated by the following symbols: s (singlet), d (doublet) and m (multiplet).

¹H and ¹³C NMR spectra of compounds **4a–m**,^[20] **5a–g**^[21] and **6a–h**^[22] have previously been described.

Chloro-di-(2-methylphenyl)phosphine (**1b**)

2-Bromotoluene (86.0 mmol, 10.3 mL, 2.0 equivs.) was added dropwise at room temperature to a suspension of magnesium turnings (94.6 mmol, 2.30 g, 2.2 equivs.) in dry Et₂O (40 mL). The reaction mixture was then refluxed for 3 h. After cooling to 0 °C, PCl₃ (43.0 mmol, 3.75 mL, 1.0 equiv.) was added dropwise under vigorous stirring. The reaction mixture was warmed to room temperature for 1 h. The magnesium salts were removed by filtration under a flush of argon and washed three times with Et₂O (3 × 20 mL). The organic solvent was distilled off under an atmosphere of argon and the residue was dried under vacuum (0.1 mbar) for 20 h. This yellowish oil contained **1b** (purity > 90 %) and no PCl₃ was left. ¹H NMR (400 MHz, CDCl₃): δ = 2.41 (s, 6H), 7.10–7.17 (m, 4H), 7.21–7.25 (m, 2H), 7.40–7.43 (m, 2H); ³¹P NMR (162 MHz, CDCl₃): δ = 66.9.

Chloro-di-(3-methylphenyl)phosphine (**1c**)

A solution of *t*-BuLi (1.5 M solution in pentane, 32.8 mmol, 21.9 mL, 4.1 equivs.) was added dropwise at 0 °C to a solution of 3-bromotoluene (17.6 mmol, 2.13 mL, 2.2 equivs.) in dry cyclohexane (70 mL). The reaction mixture was warmed to room temperature for 15 h. After cooling to 0 °C, PCl₂NEt₂ (8.0 mmol, 1.39 g, 1.0 equiv.) was added dropwise. The reaction mixture was stirred at room temperature for 1 h, then centrifuged (3000 rpm for 3 min) under an atmosphere of argon to remove inorganic salts. Dry HCl was then bubbled at room temperature for 5 min in the liquid phase obtained. The resulting ammonium salts were filtered off under a flush of argon. The filtrates were recovered and the organic solvents were distilled off under an atmosphere of argon. The residue was dried under vacuum (0.1 mbar) for 20 h. This yellowish oil contained **1c** (purity > 90 %) and no PCl₂NEt₂ was left. ¹H NMR (400 MHz, CDCl₃): δ = 2.27 (s, 6H), 7.12 (d, *J* = 7.3 Hz, 2H), 7.18–7.22 (m, 2H), 7.27–7.35 (m, 4H); ³¹P NMR (162 MHz, CDCl₃): δ = 84.1.

General Procedure for the Synthesis of Diarylphosphinopolystyrenes **2b** and **c**

Pieces of lithium wire (24.0 mmol, 167.0 mg) were added to solutions of **1b** and **c** (8.0 mmol) in anhydrous THF (20 mL) under an atmosphere of argon. The reaction mixtures were stirred at room temperature for 15 h. The resulting dark red

solutions were added in small portions to a suspension of a Merrifield resin (0.86 mmol of Cl, 1.0 g) in anhydrous THF (20 mL) under an atmosphere of argon. The reaction mixtures were stirred at room temperature for 72 h then quenched by addition of a 2:1 mixture of acetone/H₂O (30 mL). The resins were filtered under vacuum and washed three times with H₂O (3 × 30 mL), acetone (3 × 30 mL), CHCl₃ (3 × 30 mL), toluene (3 × 30 mL) and Et₂O (3 × 30 mL). The resins were then refluxed in a 3:1 mixture of EtOH/toluene (20 mL) for 15 h. The resins were filtered under vacuum, washed with toluene (30 mL), Et₂O (30 mL) and dried under vacuum (0.1 mbar) for 20 h.

Di-(2-methylphenyl)phosphinopolystyrene 2b: White resin. Anal. found: P 1.85, Cl < 300 ppm.

Di-(3-methylphenyl)phosphinopolystyrene 2c: White resin. Anal. found: P 2.10, Cl < 300 ppm.

General Procedure for the Syntheses of Diarylphosphinopolystyrene-Supported Palladium Catalysts 3b and c

Small portions of Pd(PPh₃)₄ (28 µmol, 32.6 mg) were added at room temperature to suspensions of **2b** and **c** (1.0 g) in anhydrous toluene (50 mL) under an atmosphere of argon. The reaction mixtures were degassed with argon and stirred at room temperature for 20 h. The resins **3b** and **c** were filtered under vacuum and washed three times with toluene (3 × 20 mL) and Et₂O (3 × 20 mL). Catalysts **3b** and **c** were dried under vacuum (0.1 mbar) for 20 h.

Di-(2-methylphenyl)phosphinopolystyrene palladium catalyst 3b: Dark red resin. Anal. found: P 1.85, Pd 0.3.

Di-(3-methylphenyl)phosphinopolystyrene palladium catalyst 3c: Brown resin. Anal. found: P 2.10, Pd 0.3.

General Procedure for the Syntheses of Biaryls 4a–m

Catalyst **3b** (23.1 mg, 0.5 mequivs. of supported palladium) was added to a solution of aryl bromide (1.30 mmol, 1.0 equiv.), arylboronic acid (1.43 mmol, 1.1 equivs.), Na₂CO₃ (1.56 mmol, 165.3 mg, 1.2 equivs.) in a mixture of toluene (5 mL), EtOH (1 mL) and H₂O (1 mL). The reaction mixture was then heated at 100 °C for 20 h. After cooling to room temperature, **3b** was filtered under vacuum. The catalyst was washed three times with AcOEt (3 × 20 mL). The organic phase was washed with H₂O (30 mL), dried with MgSO₄, filtered and concentrated under vacuum. The residue was filtered on silica gel to afford pure biaryls after drying under vacuum (0.1 mbar).

General Procedure for the Syntheses of Alkynes 5a–g

Catalyst **3b** (2.5 mequivs. or 5.0 mequivs. of supported palladium depending on the nature of the aryl iodide) was added to a solution of aryl iodide (1.30 mmol, 1.0 equiv.), alkyne (1.56 mmol, 1.2 equivs.), piperidine (1.56 mmol, 0.15 mL, 1.2 equivs.) and CuI (65.0 µmol, 12.4 mg, 50 mequivs.) in MeCN (3 mL). The reaction mixture was degassed twice with argon and heated at 80 °C for 20 h. After cooling to room temperature, the mixture was filtered under vacuum. The recovered catalyst was washed three times with AcOEt (3 × 20 mL). The organic phase was washed with a saturated solution of NH₄Cl (30 mL), dried with MgSO₄, filtered and concentrated under vacuum. The residue was filtered on

silica gel to afford pure alkynes after drying under vacuum (0.1 mbar).

General Procedure for the Syntheses of Alkenes 6a–h

Catalyst **3c** (115.0 mg, 2.5 mequivs. of supported palladium) was added to a solution of aryl iodide (1.30 mmol, 1.0 equiv.), alkene (2.60 mmol, 2.0 equivs.), Et₃N (1.56 mmol, 0.22 mL, 1.2 equivs.) in MeCN (3 mL). The reaction mixture was heated at 80 °C for 20 h. After cooling to room temperature, **3c** was filtered under vacuum. The catalyst was washed three times with AcOEt (3 × 20 mL). The organic phase was washed with a saturated solution of NH₄Cl (30 mL), dried with MgSO₄, filtered and concentrated under vacuum. The residue was filtered on silica gel to afford pure alkenes after drying under vacuum (0.1 mbar).

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