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Mizoroki–Heck Reactions Catalyzed by Dichloro{bis[1-(dicyclohexylphosphanyl)piperidine]}palladium: Palladium Nanoparticle Formation Promoted by (Water-Induced) Ligand Degradation

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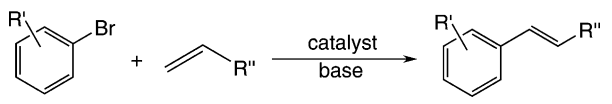
Abstract: The palladium-based dichlorobis[1-(dicyclohexylphosphanyl)piperidine] complex – $[(P\{(NC_5H_{10})(C_6H_{11})_2\})_2Pd(Cl)_2]$ is readily prepared in quantitative yield from the reaction of $[Pd(cod)(Cl)_2]$ (cod = cycloocta-1,5-diene) with two equivalents of 1-(dicyclohexylphosphanyl)piperidine in toluene under N_2 within only a few minutes at room temperature. This complex is a highly active Heck catalyst with excellent functional group tolerance, which reliably operates at low catalyst loadings. Various activated, non-activated, deactivated, functionalized, sterically hindered, and heterocyclic aryl bromides, which may contain nitro, chloro or trifluoromethane groups, nitriles, acetales, ketones, aldehydes, ethers, esters, lactones, amides, anilines, phenols, alcohols, carboxylic acids, and heterocyclic aryl bromides, such as pyridines and derivatives, as well as thiophenes and aryl bromides containing methylsulfanyl groups have been successfully coupled with various (also functionalized) alkenes in excellent yields and selectivities (the *E*-isomers are typically exclusively formed) at 140 °C in the presence of 0.05 mol% of the catalyst in DMF. Even though lower catalyst loadings could be used for many electronically activated, non-activated and some electronically deactivated aryl bromides without noticeable loss of activity, the great advantage of the reaction protocol presented here lies in its reliability and general applicability, which allows its direct adoption to other aryl bromides without the neccessity of its modification. Experimental observations indicated that palladium nanoparticles are the catalytically active form. Consequently, whereas comparable levels of activity were observed for dichloro-bis(aminophosphine) complexes of palladium, a dramatic drop in activity was found for their phosphine-based analogue $[(P(C_6H_{11})_3)_2Pd(Cl)_2]$.

Keywords: aminophosphines; C–C bond formation; Heck cross-coupling; nanoparticles; palladium

Introduction

The Mizoroki–Heck reaction belongs to an indispensable set of palladium-catalyzed cross-coupling reactions and is nowadays the method of choice for the arylation of alkenes (Scheme 1).[1] Various types of palladium complexes have been reported to promote the vinylation of aryl halides, of which many follow the "classical" Pd(0)/Pd(II) mechanism,[2] as it is, for example, the case for species $[Pd(PPh_3)_4]$ or $[Pd(PPh_3)_2(OAc)_2]$.[3] Other systems, such as $[Pd(OAc)_2]$, serve as sources of palladium nanoparticles.[4] In the case of pincer-type complexes, which have been introduced in the late 1990s as Heck catalysts,[5–7] nanoparticles are generally considered to be their catalytically active form, even though the often proposed controversial Pd(II)/Pd(IV) cycles still cannot be excluded completely as being operative.[8] In contrast, recent experimental and computational investigations indicated that pincer-type Pd(IV) intermediates are thermally accessible and hence, are to be considered as reactive intermediates in reactions performed with aryl halides in polar, non-protic solvents and at elevated temperatures.[9,10]



Scheme 1. General scheme of a Heck cross-coupling reaction between an aryl bromide and an olefin.

Although recent developments led to a considerable increase in the activity of Heck catalysts, of which some efficiently couple sterically hindered substrates or occasionally even aryl chlorides (in the absence of aryl bromide units) under mild reaction conditions, a typical protocol for this reaction still requires prolonged reaction times and relatively high catalyst loadings. Moreover, in most cases only few reactions with rather simple substrates and coupling partners have been tested. In addition, modified reaction conditions (reaction temperatures, catalyst loadings, additives, e.g.) are often reported for different substrates, which strongly limit their application in organic synthesis or industrial processes. Furthermore, the catalyst syntheses are often time consuming, difficult, and/or require the use of expensive starting materials and many of these catalysts suffer from poor thermal stability, low functional group tolerance and/or sensitivity towards both, air and moisture, and hence require inconvenient inert-atmosphere techniques for their successful use, which demonstrates the clear need for more efficient and definitely more generally applicable systems.

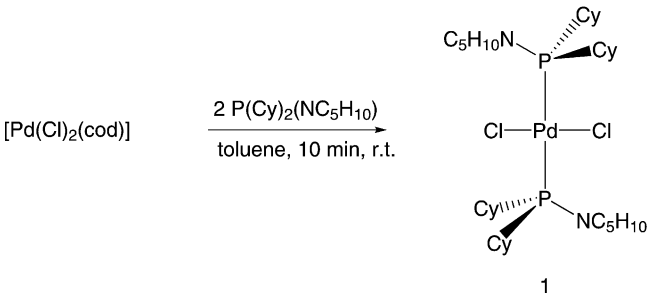
We report herein the catalytic activity of dichlorobis[1-(dicyclohexylphosphanyl)piperidine]palladium, $[(P\{(NC_5H_{10})(C_6H_{11})_2\})_2Pd(Cl)_2]$ (**1**), in the arylation of olefins performed with a wide variety of activated, non-activated, deactivated and sterically hindered, functionalized as well as heterocyclic aryl bromides and various different types of olefins, which reliably operates at low catalyst loadings and thus, demonstrates its general applicability in this process. We show that **1** is a highly efficient and extremely versatile Heck catalyst with an excellent functional group tolerance, which exclusively activates C_{aryl}–Br bonds when bromochlorobenzenes were applied. Excellent conversions and product yields were typically obtained within a few hours of reaction time. Moreover, the *E*-isomer of the arylated olefins is often exclusively formed. Even though extremely low catalyst loadings could be used for many of the cross-coupling reactions performed without loss of activity or reliability, all the reactions examined have been described with a single catalyst under uniform reaction conditions (at 140 °C in DMF and K_2CO_3 as solvent and base and in the presence of 0.05 mol% of catalyst), which allows a direct adoption of the reaction protocol presented here to other aryl bromides without the neccessity of its modification. Overall, **1** is nowadays one of the most effective and versatile catalyst for the vinylation of aryl bromides and thus, a real alternative to the currently applied Heck catalysts.

Aminophosphine-based complexes of the type $[(P\{(NC_5H_{10})_{3-n}(C_6H_{11})_n\})_2Pd(Cl)_2]$ ($n=0$–2) were assumed to be ideal Heck catalysts, because they proved to promote (in contrast to phosphine-based systems) efficiently the formation of palladium nanoparticles (nanoparticles were shown to be the catalytically active form in the Suzuki reaction) as well as being able to operate *via* homogeneous mechanisms, as it was recently demonstrated in Negishi cross-coupling reactions.[11] Consequently, whereas a similar catalytic activity will be found for the aminophosphine-based system when compared to their phosphine-based analogues in a homogeneous mechanism, a significantly improved catalytic activity was expected to be obtained when palladium nanoparticles are the true catalytically active form. Experimental observations strongly indicate that palladium nanoparticles are involved in the catalytic cycle of the Heck reaction performed with complexes of type $[(P\{(NC_5H_{10})_{3-n}(C_6H_{11})_n\})_2Pd(Cl)_2]$ ($n=0$–2) under the chosen reaction conditions and thus, provide a simple explanation why comparable catalytic activities were found for the aminophosphine-based systems while a dramatic drop in activity was found for their phosphine-based analogues.

Results and Discussion

Catalyst preparation

Treatment of toluene suspensions of $[Pd(Cl)_2(cod)]$ (cod = cycloocta-1,5-diene) with two equivalents of 1-(dicyclohexylphosphanyl)piperidine under N_2 at 25 °C exclusively and quantitatively yielded within few minutes the dichlorobis[1-(dicyclohexylphosphanyl)-piperidine] complex of palladium, namely $[(P\{(NC_5H_{10})(C_6H_{11})_2\})_2Pd(Cl)_2]$ (**1**) (Scheme 2).[11a]

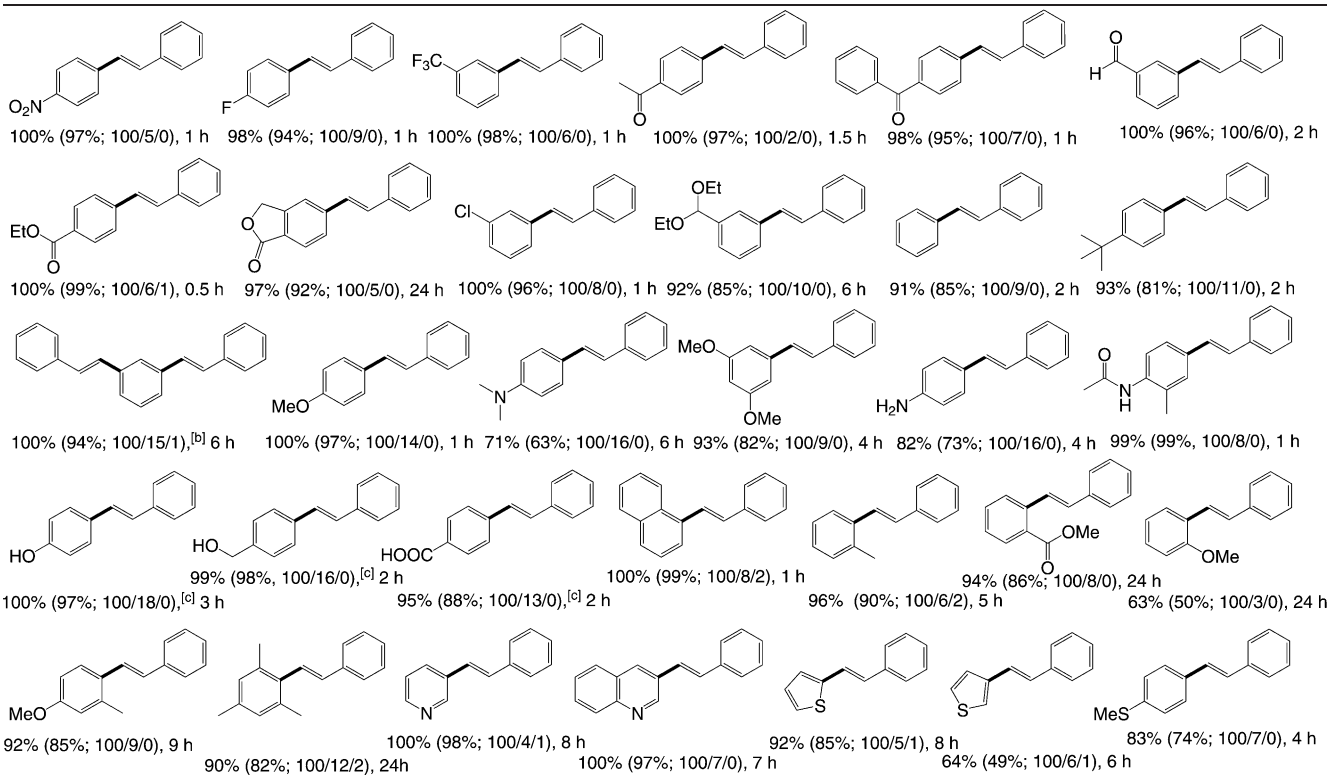


Scheme 2. Synthesis of dichloro{bis[1-(dicyclohexylphosphanyl)piperidine]}palladium (**1**).

Catalysis

Complex **1** is a highly active, reliable, and versatile Heck catalyst with excellent functional group tolerance, that successfully couples a large variety of aryl bromides which may contain nitro, chloro or trifluoromethane groups, nitriles, acetales, ketones, aldehydes, ethers, esters, lactones, amides, anilines, phenols, alcohols, carboxylic acids, and heterocyclic aryl bromides,

Table 1. Heck cross-coupling reactions between aryl bromides and styrene, catalyzed by **1**.[a]



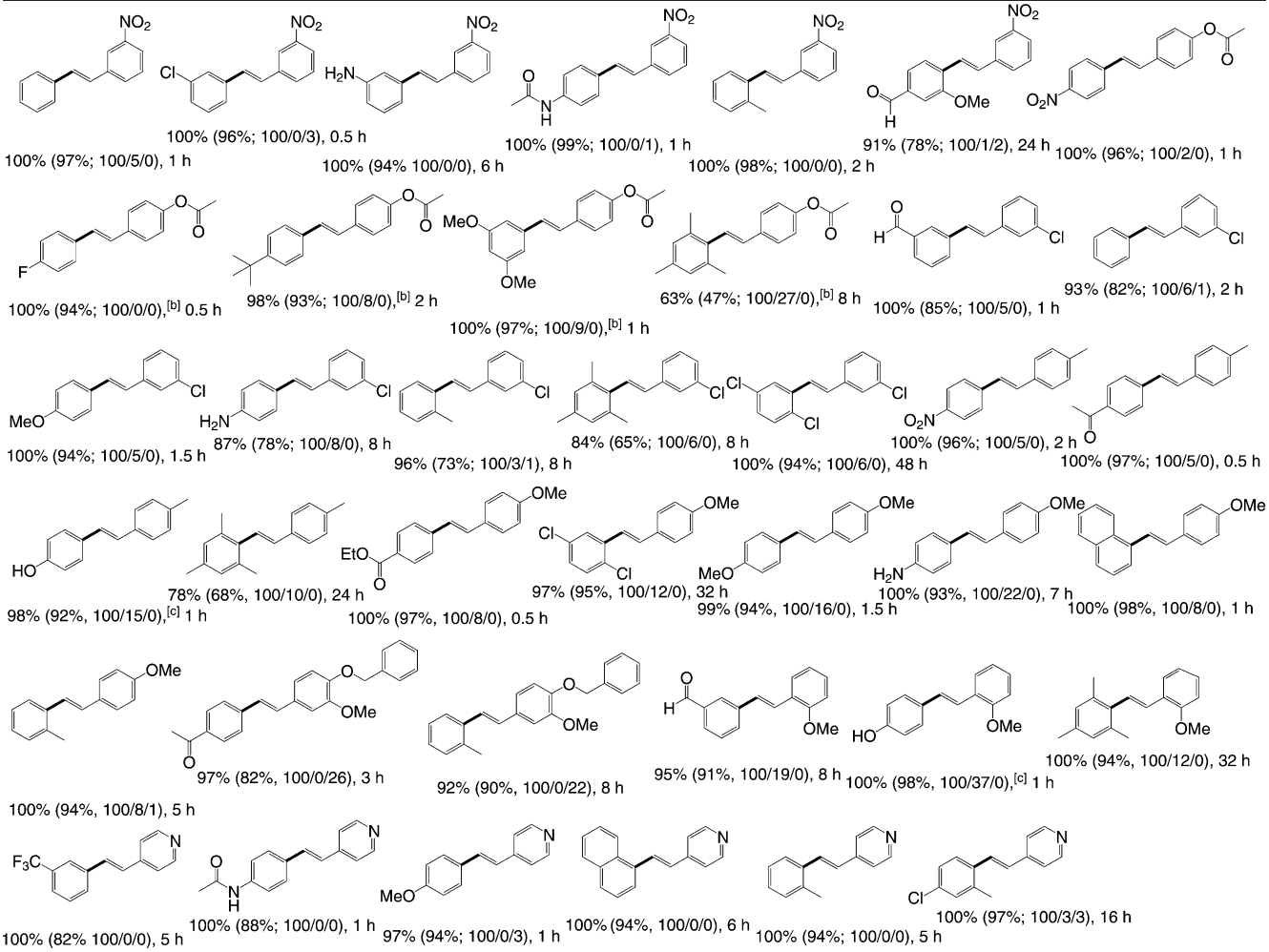
[a] *Reaction conditions:* 1.0 mmol aryl bromide, 1.5 mmol olefin (relative to bromide), 2.0 mmol K_2CO_3, 2.5 mL DMF, catalyst (0.05 mol%) added in solution (THF), reaction performed at 140 °C. The conversions and product ratios (*trans*/*gem*/*cis*) are determined by GC/MS, based on aryl bromide, isolated yields are given in brackets.

[b] The product ratio refers to (*trans-trans*/*trans-gem*/*trans-cis*).

[c] 3.0 mmol of K_2CO_3 were used.

such as pyridines and derivatives, as well as thiophenes and aryl bromides containing methylsulfanyl groups with various (also functionalized) alkenes in excellent yields – generally within few hours at 140 °C in DMF and K_2CO_3 as solvent and base in the presence of only 0.05 mol% of catalyst. Exemplary cross-coupling reactions were performed with styrene (Table 1) and its derivatives, such as 1-ethenyl-4-methylbenzene, 1-ethenyl-4-methoxybenzene, 1-ethenyl-3-nitrobenzene, 1-ethenyl-3-chlorobenzene, 4-ethenylphenyl acetate, 1-(benzyloxy)-4-ethenyl-2-methoxybenzene, and 1-ethenyl-2-methoxybenzene as well as 4-vinylpyridine (Table 2). Further reactions have been performed with *N*,*N*-dimethylprop-2-enamide, 4-acryloylmorpholine (Table 3), and butyl prop-2-enoate (Table 4). Notably, the base, solvent and reaction temperature strongly influence the conversion rates and yields: whereas best results were observed with K_2CO_3, for example, the use of K_3PO_4, sodium acetate or potassium *tert*-butoxide is not appropriate and led to very low conversion rates and yields – among other reasons, due to fast deposition of inactive palladium black. Also the use of amines, such as NEt_3 and pyridine is not practical due to their ligating properties and inhibits the catalysis efficiently. A similar effect was found by a change of solvent: while only a slightly lower catalytic activity was noticed in NMP, replacement of DMF by (non-polar) *p*-xylene, for example, leads to a dramatic drop of activity. Almost no catalytic activity was obtained when the Heck reactions were performed in DMSO or *n*-butanol. Finally, lowered reaction temperatures retard the conversions significantly. However, when styrene was allowed to react at 140 °C in DMF and K_2CO_3 as solvent and base in the presence of 0.05 mol% of catalyst with electronically activated non-*ortho*-substituted aryl bromides, the desired product was quantitatively formed within 2 h (Table 1). Exemplary reactions have been performed with 1-bromo-4-nitrobenzene, 1-bromo-4-fluorobenzene, 1-bromo-3-(trifluoromethyl)benzene, 1-(4-bromophenyl)ethanone, (4-bromophenyl)(phenyl)methanone, and 3-bromobenzaldehyde as well as 1-bromo-3-(diethoxymethyl)benzene, and 1-bromo-3-chlorobenzene, of which the latter exclusively yielded 1-chloro-3-[(*E*)-2-phenylethenyl]benzene. Essentially the same conversion

Table 2. Heck cross-coupling reactions between aryl bromides and derivatives of styrene, catalyzed by **1**.[a]



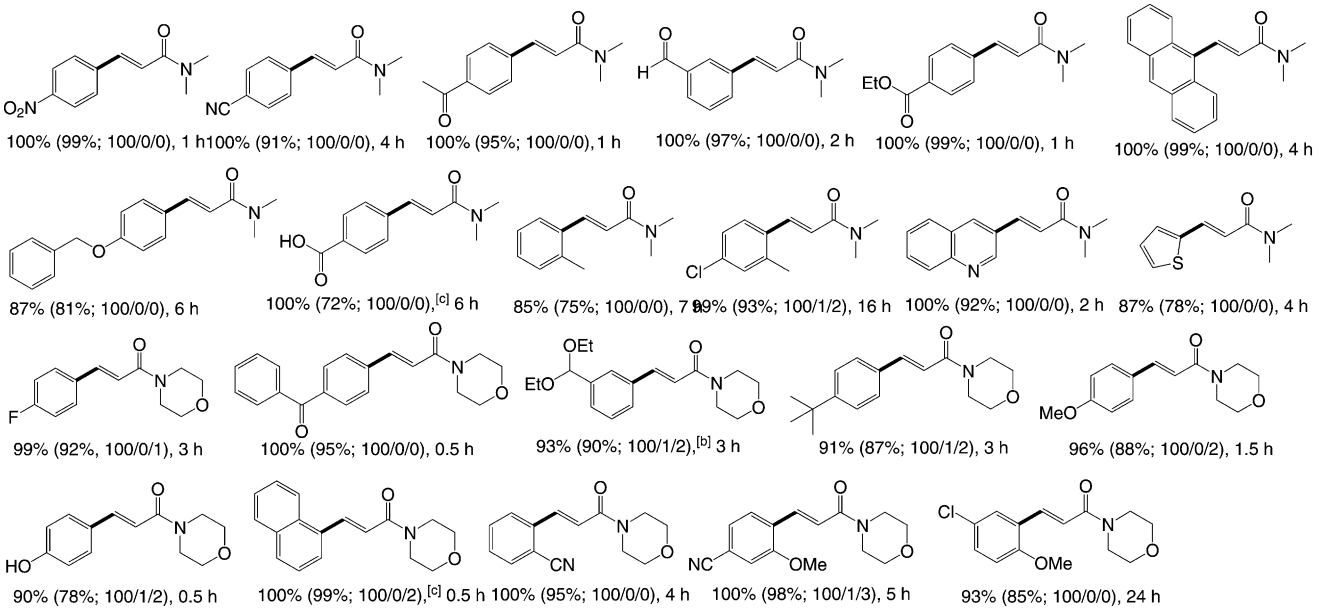
[a] *Reaction conditions:* 1.0 mmol aryl bromide, 1.5 mmol olefin (relative to bromide), 2.0 mmol K_2CO_3, 2.5 mL DMF, catalyst (0.05 mol%) added in solution (THF), reaction performed at 140 °C. The conversions and product ratios (*trans*/*gem*/*cis*) are determined by GC/MS, based on aryl bromide, isolated yields are given in brackets.

[b] Isolated as phenol.

[c] 3.0 mmol of K_2CO_3 were used.

rates and yields were achieved when non-activated aryl bromides were applied. Examples include reactions performed with bromobenzene and 1-bromo-4-*tert*-butylbenzene. Slow but quantitative product formation (24 h were required for full conversion) was noticed for the conversion of 5-bromo-2-benzofuran-1(3*H*)-one into 5-[(*E*)-2-phenylethenyl]-2-benzofuran-1(3*H*)-one. However, an excellent performance was also observed when aryl bromides with an increased electron density on the aryl unit were applied. Exemplary reactions have been performed with 1-bromo-4-methoxybenzene, 4-bromo-*N*,*N*-dimethylaniline as well as with 1-bromo-3,5-dimethoxybenzene, which cleanly yielded the respective coupling products in almost quantitative yields. Further reactions have been performed with 4-bromoaniline, 4-bromophenol, (4-bromophenyl)methanol and 4-bromobenzoic acid, which were successfully converted into 4-[(*E*)-2-phenylethenyl]aniline, 4-[(*E*)-2-phenylethenyl]phenol, {4-[(*E*)-2-phenylethenyl]phenyl}methanol and 4-[(*E*)-2-phenylethenyl]benzoic acid, respectively. The product yields were in all the reactions higher than 82%, of which the *E*-isomer was formed in >90%. The same yields but prolonged reaction times were noticed when sterically hindered aryl bromides were applied: For example, when 1-bromonaphthalene, 1-bromo-2-methylbenzene, methyl 2-bromobenzoate or 2-bromo-1,3,5-trimethylbenzene were used as substrates, the respective coupling products were cleanly formed and could have been isolated in excellent yields. Moreover, also heterocyclic aryl bromides were successfully used as substrates. Examples include reactions with 3-

Table 3. Heck cross-coupling reactions between aryl bromides and *N*,*N*-dimethylprop-2-enamide, and 4-acryloylmorpholine, catalyzed by **1**.[a]



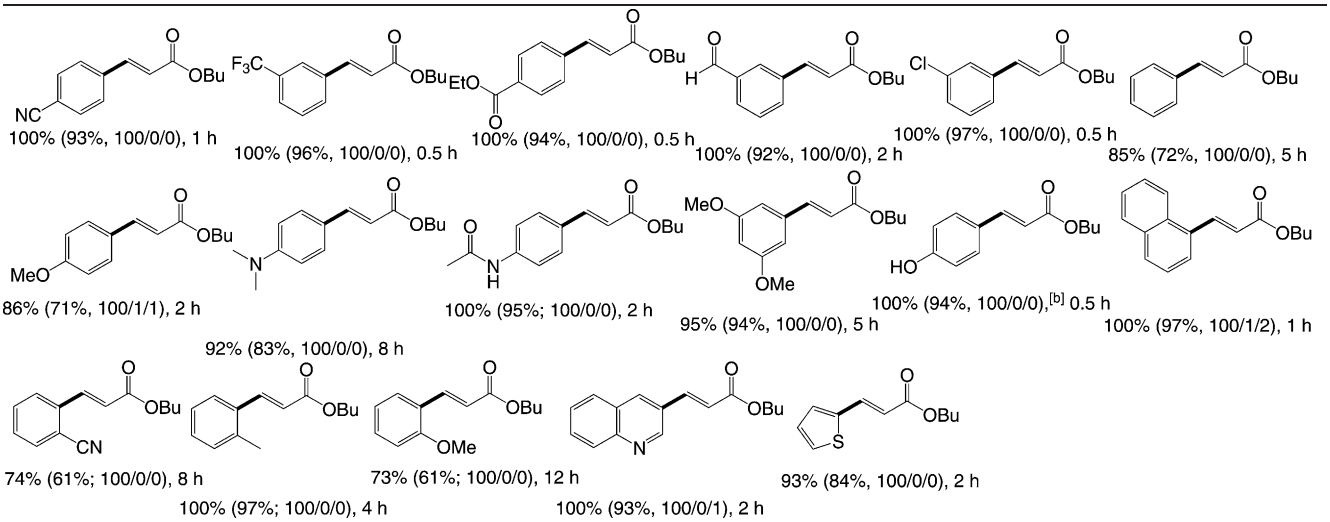
[a] *Reaction conditions:* 1.0 mmol aryl bromide, 1.5 mmol olefin (relative to bromide), 2.0 mmol K_2CO_3, 2.5 mL DMF, catalyst (0.05 mol%) added in solution (THF), reaction performed at 140 °C. The conversions and product ratios (*trans*/*gem*/*cis*) are determined by GC/MS, based on aryl bromide, isolated yields are given in brackets.

[b] Isolated as the aldehyde.

[c] 3.0 mmol of K_2CO_3 were used.

bromopyridine and 3-bromoquinoline, which undergo clean and quantitative conversion into 3-[(*E*)-2-phenylethenyl]pyridine and 3-[(*E*)-2-phenylethenyl]quinoline within 8 h. The coupling products were isolated in almost quantitative yields. An excellent performance was also obtained when sulphur-containing substrates were applied: For example, whereas 94% conversion of 2-bromothiophene into the respective coupling product was achieved in 8 h, 64% conversion into 3-[(*E*)-2-phenylethenyl]thiophene was achieved in 6 h with 3-bromothiophene as substrate. A similar performance was generally noticed when derivatives of styrene were used as coupling partners (Table 2). For example, when 1-ethenyl-3-nitrobenzene was used as coupling partner, complete and almost exclusive formation of the *E*-isomers was typically achieved within 2 h. Exemplary reactions were performed with bromobenzene, 1-bromo-3-chlorobenzene, and *N*-(4-bromophenyl)acetamide. High conversions were also achieved when sterically hindered aryl bromides, such as 1-bromo-2-methylbenzene or 4-bromo-3-methoxybenzaldehyde were coupled with 1-ethenyl-3-nitrobenzene, which afforded 1-methyl-2-[(*E*)-2-(3-nitrophenyl)ethenyl]benzene and 3-methoxy-4-[(*E*)-2-(3-nitrophenyl)ethenyl]benzaldehyde, respectively, in 98 and 78% yields. However, whereas formation of the former was complete after 2 h, 24 h were required for the latter. Essentially the same conversion rates, product yields and selectivities were obtained when 4-ethenylphenyl acetate, 1-ethenyl-3-chlorobenzene, 1-ethenyl-4-methylbenzene, and 1-ethenyl-4-methoxybenzene – a styrene derivative with an increased electron density on the aryl unit – were used as coupling partners. Exemplary reactions have been performed with electronically activated aryl bromides, such as 1-bromo-4-fluorobenzene, 1-bromo-4-nitrobenzene, 1-(4-bromophenyl)ethanone, electronically deactivated 1-bromo-3,5-dimethoxybenzene, *N*-(4-bromophenyl)acetamide, 4-bromophenol as well as sterically hindered 1-bromonaphthalene, 1-bromo-2-methylbenzene, and 2-bromo-1,3,5-trimethylbenzene. The same yields but retarded conversions have been noticed when the cross-coupling reactions were performed with electron-rich olefins, such as 1-(benzyloxy)-4-ethenyl-2-methoxybenzene or sterically hindered olefins, like 1-ethenyl-2-methoxybenzene. Exemplary reactions have been performed with 1-(4-bromophenyl)ethanone, 3-bromobenzaldehyde 4-bromophenol, 1-bromo-2-methylbenzene, and 2-bromo-1,3,5-trimethylbenzene. Further retardation was noticed with 4-vinylpyridine as coupling partner. For example, reactions performed with 1-bromo-3-(trifluoromethyl)benzene, *N*-(4-bromophenyl)acetamide, 1-bromo-4-methoxybenzene, 1-bromonaphthalene and

Table 4. Heck cross-coupling reactions between aryl bromides and butyl prop-2-enoate, catalyzed by **1**.[a]



[a] *Reaction conditions:* 1.0 mmol aryl bromide, 1.5 mmol olefin (relative to bromide), 2.0 mmol K_2CO_3, 2.5 mL DMF, catalyst (0.05 mol%) added in solution (THF), reaction performed at 140 °C. The conversions and product ratios (*trans*/*gem*/*cis*) are determined by GC/MS, based on aryl bromide, isolated yields are given in brackets.

[b] 3.0 mmol of K_2CO_3 were used.

1-bromo-2-methylbenzene quantitatively yielded the coupling products within 6 h. It should be emphasized that the C_{aryl}–Br bonds are exclusively activated when bromochlorobenzenes were applied. For example, when 2-bromo-1,4-dichlorobenzene was coupled with 1-ethenyl-4-methoxybenzene or 1-ethenyl-3-chlorobenzene full conversion into 1,4-dichloro-2-[(*E*)-2-(4-methoxyphenyl)ethenyl]benzene and 1,4-dichloro-2-[(*E*)-2-(3-chlorophenyl)ethenyl]benzene was achieved after 32 and 48 h, respectively. Similarly, 4-[(*E*)-2-(4-chloro-2-methylphenyl)ethenyl]pyridine was exclusively and quantitatively formed within 16 h when 1-bromo-4-chloro-2-methylbenzene was coupled with 4-vinylpyridine. Finally, when 2-bromo-1,3-dichlorobenzene was coupled with 1-ethenyl-4-methylbenzene, 80% conversion into 1,3-dichloro-2-[(*E*)-2-(4-methylphenyl)ethenyl]benzene was achieved after 24 h, while only ~4% of 1-chloro-2,3-bis[(*E*)-2-phenylethenyl]benzene was detectable.

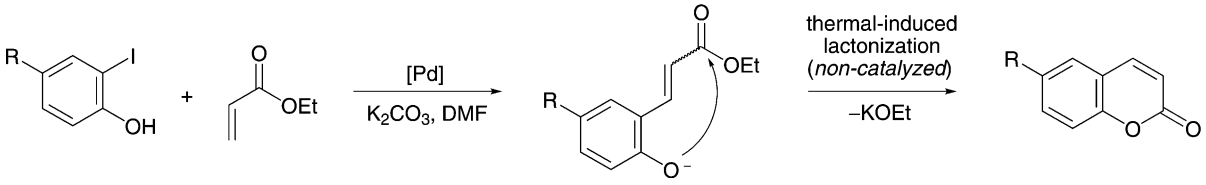
An excellent performance and thus, clean, quantitative and highly selective product formations within short reaction times was generally observed when *N*,*N*-dimethylprop-2-enamide and 4-acryloylmorpholine were used as coupling partners (Table 3). Exemplary reactions have been performed with electronically activated, non-activated or deactivated aryl bromides, such as 1-bromo-4-nitrobenzene, 4-bromobenzonitrile, 1-(4-bromophenyl)ethanone, ethyl 4-bromobenzoate, 3-bromobenzaldehyde, 9-bromoanthracene, and 1-(benzyloxy)-4-bromobenzene as well as with sterically hindered, functionalized and heterocyclic substrates, such as 1-bromo-2-methylbenzene, 2-bromobenzonitrile, 4-bromo-3-methoxybenzonitrile, 4-bromophenol, 4-bromobenzoic acid, 3-bromoquinoline and 2-bromothiophene, which in all the reactions examined exclusively yielded the *E*-isomers in excellent yields. For example, when *N*,*N*-dimethylprop-2-enamide was coupled with 3-bromobenzaldehyde, (2*E*)-3-(3-formylphenyl)-*N*,*N*-dimethylprop-2-enamide was exclusively and quantitatively formed in 2 h. The isolated yield was 97%. Furthermore, whereas full conversions of 1-bromo-4-nitrobenzene, 1-(4-bromophenyl)ethanone, and ethyl 4-bromobenzoate into (2*E*)-*N*,*N*-dimethyl-3-(4-nitrophenyl)prop-2-enamide, (2*E*)-3-(4-acetylphenyl)-*N*,*N*-dimethylprop-2-enamide, and ethyl 4-[(1*E*)-3-(dimethylamino)-3-oxoprop-1-en-1-yl]benzoate, respectively, were achieved within 1 hour, a slightly prolonged reaction time (4 h) was required for the quantitative formation of (2*E*)-3-(4-cyanophenyl)-*N*,*N*-dimethylprop-2-enamide. The same yields but a slightly reduced catalytic activity were noticed when sterically hindered aryl bromides were used as substrates. An excellent performance was also noticed with heterocyclic substrates, such as 2-bromothiophene and 3-bromoquinoline, which were smoothly converted into (2*E*)-*N*,*N*-dimethyl-3-thiophen-2-ylprop-2-enamide and (2*E*)-*N*,*N*-dimethyl-3-quinolin-3-ylprop-2-enamide within only 4 and 2 h, respectively. Exclusive C_{aryl}–Br bonds activation and thus, quantitative formation of (2*E*)-3-(4-chloro-2-methylphenyl)-*N*,*N*-dimethylprop-2-enamide was observed in 16 h when 1-bromo-4-chloro-2-methylbenzene was applied. The same performance was generally observed with 4-acryloylmorpholine as coupling partner.

Essentially the same performance was noticed with butyl prop-2-enoate as coupling partner (Table 4). For example, when ethyl 4-bromobenzoate or 1-bromo-3-(trifluoromethyl)benzene was coupled with butyl prop-2-enoate, ethyl 4-[(1*E*)-3-butoxy-3-oxoprop-1-en-1-yl]benzoate and butyl (2*E*)-3-[3-(trifluoromethyl)phenyl]prop-2-enoate were cleanly and quantitatively formed within only 30 min. Moreover, butyl (2*E*)-3-(3-chlorophenyl)prop-2-enoate was exclusively and quantitatively formed in 30 min when 1-bromo-3-chlorobenzene was used as substrate. A slightly retarded conversion was noticed for 4-bromobenzonitrile and 3-bromobenzaldehyde: Whereas full conversion of the former into butyl (2*E*)-3-(4-cyanophenyl)-prop-2-enoate was achieved in 1 hour, 2 h were required for the quantitative formation of butyl 3-formylbenzoate. The same yields but further retardations were noticed when non-activated and deactivated aryl bromides, such as bromobenzene, 1-bromo-4-methoxybenzene, 4-bromo-*N*,*N*-dimethylaniline or 1-bromo-3,5-dimethoxybenzene were coupled with butyl prop-2-enoate. Interestingly, even though complete conversion of *N*-(4-*b*romophenyl)acetamide into butyl 4-(acetylamino)cinnamate was obtained and thus, a product yield of 95% was achieved after 2 h, it is worth mentioning that GC/MS analysis of the reaction mixture (after 30 min) indicated the reversible formation of potassium (1*Z*)-3-(acetyl{4-[(1*E*)-3-butoxy-3-oxoprop-1-en-1-yl]phenyl}amino)-1-butoxy-prop-1-en-1-olate, a Michael-type product between potassium acetyl{4-[(1*E*)-3-butoxy-3-oxoprop-1-en-1-yl]phenyl}azanide, the deprotonated form of the Heck product {butyl (2*E*)-3-[4-(acetylamino)phenyl]prop-2-enoate]} and butyl prop-2-enoate. However, when sterically hindered substrates, such as 1-bromo-2-methylbenzene, 2-bromobenzonitrile or 1-bromo-2-methoxybenzene were coupled with butyl prop-2-enoate retarded conversions were generally observed in the Heck reaction. Moreover, their conversion into butyl (2*E*)-3-(2-methylphenyl)prop-2-enoate, butyl (2*E*)-3-(2-cyanophenyl)prop-2-enoate and butyl (2*E*)-3-(2-methoxyphenyl)prop-2-enoate, respectively, was accompanied by the formation of a by-product (as indicated by GC/MS analysis of the reaction mixtures). Anyhow, since the by-product was in all these reactions the same, the involvement of aryl bromides in its formation could have been excluded. Indeed, thermal treatment of DMF solutions of butyl prop-2-enoate (in the presence of K_2CO_3 but in the absence of aryl bromide and catalyst) afforded – among others – the same by-product, whose identity is unknown as yet.

Tandem Heck/Cyclization Reactions with 2-Iodophenols

Impressively, when 4-bromophenol, an electronically deactivated aryl bromide was coupled with butyl prop-2-enoate; full conversion into butyl (2*E*)-3-(4-hydroxyphenyl)prop-2-enoate was achieved within only 30 min. In contrast, when 2-bromophenol was applied, only 15% conversion into butyl (2*E*)-3-(2-hydroxyphenyl)prop-2-enoate was achieved within 24 h. Moreover, among other products, 20% of 2*H*-chromen-2-one (coumarine) had formed, most probably *via* cyclization of butyl (2*E*)-3-(4-hydroxyphenyl)-prop-2-enoate. 2*H*-Chromen-2-ones, however, are important synthetic targets, as they are integral parts in various complex natural products with pharmacological activities, such as anticancer and anti-HIV activity,[12] and also have been used as photostable laser dyes, luminescent probes, and triplet sensitizers.[13] Apart from classical synthetic paths involving Perkin, Knoevenagel or Pechmann reactions, which suffer from significant drawbacks, such as the need of harsh reaction conditions, multi-step procedures, inconvenient work-up procedures and stoichiometric amounts of Lewis or inorganic acids, transition metal-catalyzed procedures have been developed to broaden their synthetic accessibility.

Nevertheless, many of these methods are limited in scope and involve the functionalization of pre-formed coumarine units or alkyne-based cyclizations,[14] this is why we were intrigued by the possibility to get a direct synthetic access to 2*H*-chromen-2-one *via* Heck/lactonization sequences (Scheme 3) from 2-iodophenols and ethyl prop-2-enoate, for which higher conversion rates and cleaner product formations were expected to be obtained when compared to reactions performed with 2-bromophenols and butyl prop-2-enoate.[15] This was tested by thermal treatment of 2-

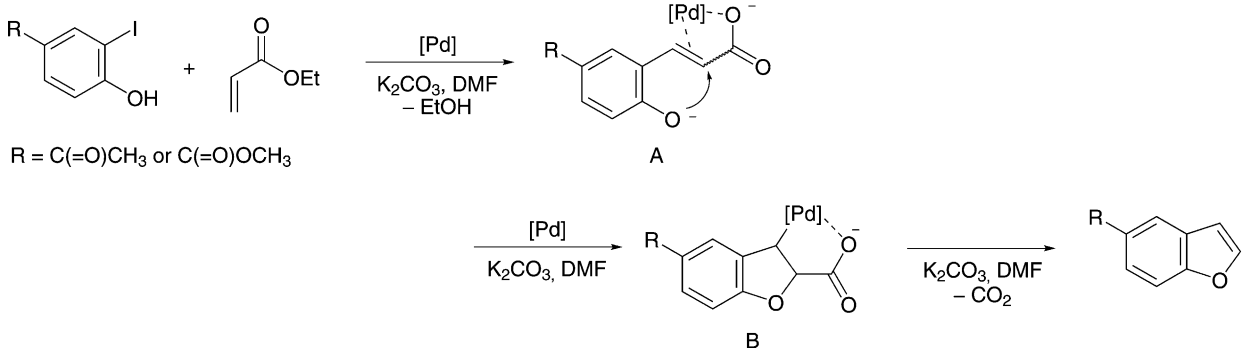


Scheme 3. 2*H*-Chromen-2-one formation *via* Heck/lactonization reaction sequences performed with 2-iodophenol and 3-iodobiphenyl-4-ol and ethyl prop-2-enoate at 140 °C in DMF and K_2CO_3 as solvent and base in the presence of 0.05 mol% of **1**.

iodophenol with an equimolar amount of ethyl prop-2-enoate in DMF and K_2CO_3 as solvent and base in the presence of 0.05 mol% of **1**. Indeed, the respective 2*H*-chromen-2-one was exclusively formed in almost quantitative yield within 24 h. Moreover, ethyl (2*E*)-3-(2-hydroxyphenyl)prop-2-enoate and ethyl (2*Z*)-3-(2-hydroxyphenyl)prop-2-enoate, the respective Heck products were clearly identified as intermediate products, of which both isomers are fully converted into coumarine by a *non-catalytic*, *thermally-induced* cyclization.[16] The same reactivity pattern and hence, formation of 6-phenyl-2*H*-chromen-2-one was obtained when 3-iodobiphenyl-4-ol was applied. On the other hand, when Heck/cyclization reactions were examined with electronically activated 1-(4-hydroxy-3-iodophenyl)ethanone or methyl 4-hydroxy-3-iodobenzoate, not 6-acetyl-2*H*-chromen-2-one and methyl 2-oxo-2*H*-chromene-6-carboxylate, but 1-(1-benzofuran-5-yl)ethanone and methyl 1-benzofuran-5-carboxylate were formed instead (Scheme 4). The substituent on the aryl unit apparently determines the reactivity pattern of the alkyl 3-(2-hydroxyaryl)prop-2-enoate intermediate and hence, the product formation: whereas for non-activated (and most probably also for deactivated) alkyl 3-(2-hydroxyaryl)prop-2-enoates an *intramolecular* lactonization process and consequently the formation of 2*H*-chromen-2-ones is favoured, an *intermolecular* nucleophilic attack of hydroxide anions (hydroxide ions are generated from the equilibrium between HCO_3^-, OH^- and CO_2)[17] on the carbonyl carbon atom and hence, the formation of the respective 3-(2-hydroxyaryl)prop-2-enoates occur when electronically activated 2-iodophenols were applied. Subsequent formation of palladium olefin complexes of type **A** promotes an *intramolecular* cyclization and thus, the formation of intermediates of type **B**. Decarboxylation of **B**, promoted by the presence of electron-withdrawing groups and subsequent reductive elimination yield the respective benzofuran. The catalyst is most probably regenerated by reduction of CO_2 (and the formation of dianionic oxalic acid). Notably, benzofurans and their analogues constitute a large family of compounds with biological and pharmaceutical activity and hence, are important synthetic targets, which are typically prepared *via* oxidative cyclization of *o*-vinylphenols,[18] dehydrative cyclization of α-phenoxy ketones,[19] cyclization of *o*-ynylphenol,[20] copper- or palladium-catalyzed O-arylation of *o*-halobenzyl ketones[21] or intramolecular McMurry couplings and Wittig reactions.[22] Palladium-catalyzed syntheses of benzofuran and its derivatives from 3-(2-hydroxyaryl)prop-2-enoates or 3-(2-hydroxyaryl)prop-2-enoic acids, however, have not been described so far and hence, are novel, offering a new synthetic approach for this important class of compounds from simple and readily available starting materials. Further investigations are ongoing.

Catalytic Performance

Dichloro{bis[1-(dicyclohexylphosphanyl)piperidine]}-palladium (**1**) belongs nowadays to the most active, versatile, and convenient Heck catalysts reported, enable a wide variety of aryl bromides, which may contain nitro, chloro or trifluoromethane groups, nitriles, acetales, ketones, aldehydes, ethers, esters, lactones, amides, anilines, phenols, alcohols, carboxylic acids, as well as heterocyclic aryl bromides, such as pyridines and derivates, or thiophenes and aryl bromides with methylsulfanyl groups to be selectively coupled with various (also functionalized) olefins in very high conversion rates and yields with only 0.05 mol% of catalyst within a few hours in DMF at 140 °C. Demonstration of such a broad functional group tolerance and applicability of a single catalyst under uniform reaction conditions is unprecedented. With this regard, it is important to note that although catalyst loadings between 0.002 and 0.01 mol% could be used for most of the reactions performed with electronically activated, non-activated and even some electronically deactivated aryl bromides without loss



Scheme 4. Palladium-catalyzed benzofuran formation *via* Heck/cyclization reaction sequences performed with (electronically activated) 1-(4-hydroxy-3-iodophenyl)ethanone and methyl 4-hydroxy-3-iodobenzoate and ethyl prop-2-enoate at 140 °C in DMF and K_2CO_3 as solvent and base in the presence of 0.1 mol% of **1**.

of activity or reliability, catalyst loadings between 0.01 and 0.05 mol% were required when sterically hindered substrates were applied. Therefore, all the reactions have been examined in the presence of 0.05 mol% of catalyst, as a universally applicable reaction protocol is more attractive (than substrate-optimized reaction conditions) for synthetic chemists or industrial applications as this allows its direct adaption to other substrates without the necessity of its modification. This is also the reason why all the reactions have been described with **1**, even though a higher level of activity was often found for dichloro-{bis[1,1′,1″-(phosphanetriyl)tripiperidine]}palladium (**2**) when electronically activated or non-activated aryl bromides or bromopyridines were used as substrates. The overall improved catalytic activity of **1** when compared with **2** {and dichloro-bis[1,1′-(cyclohexylphosphanediyl)dipiperidine]palladium (**3**)} was attributed to its higher stability, which results in a retarded palladium nanoparticle formation. Even though this also leads to prolonged induction periods, the nanoparticles are more active because their growth is slower and hence, their size smaller, which makes the ratio between palladium on the outer rim and on the inside of the particles more favourable. Consequently, whereas electronically activated and non-activated substrates or bromopyridines were more efficiently converted into the respective coupling products with **2**, significantly improved conversion rates and yields were observed with **1** when electronically deactivated or sterically hindered aryl bromides were applied. For example, while full conversion of 1-bromo-3-(trifluoromethyl)benzene or 3-bromoquinoline into 1-[(*E*)-2-phenylethenyl]-3-(trifluoromethyl)benzene and 3-[(*E*)-2-phenylethenyl]quinoline was achieved in 1 and 7 h, respectively, with **1**, only 30 min and 4 h were required to quantitatively form the cross-coupling products with **2**. On the other hand, whereas 82% of 4-bromoaniline was converted into 4-[(*E*)-2-phenylethenyl]aniline after 4 h with **1**, only ~18% of the coupling product was achieved with **2**. Similarly, while 96% conversion of 2-bromotoluene into 1-methyl-2-[(*E*)-2-phenylethenyl]benzene was obtained after 5 h with **1**, only 60% conversion was achieved with **2**.

The exceptional high catalytic performance of **1** in the Heck reaction was demonstrated further in exemplary "large-scale" reactions, where bromobenzene (52.7 mL; 0.5 mol), 1-bromonaphthalene (70 mL; 0.5 mol) and electronically deactivated 4-bromoanisole (62.5 mL; 0.5 mol) were coupled with styrene (86 mL; 0.75 mol) in 300 mL of DMF at 140 °C in the presence of K_2CO_3 (138 g; 1 mol) and only 0.0001 mol% (1 ppm) of catalyst. Impressively, 1,1′-(*E*)-ethene-1,2-diyldibenzene, 1-[(*E*)-2-phenylethenyl]naphthalene, and 1-methoxy-4-[(*E*)-2-phenylethenyl]benzene all were exclusively formed in yields between 80 and 95% and reaction times between 36 h and one week. This demonstrates on one hand the excellent catalytic activity of **1** but on the other hand also its long active lifetime and thus, the potential application of **1** in the preparation of pharmaceutically active compounds.[23,24]

Overall, **1** is in nearly all the coupling reactions performed with aryl bromides more efficient than reported for $[Pd(OAc)_2]$,[25] $[(PC^{NHC}P)Pd(Cl)][Cl]$,[26] ($\{C_6H_3$-2,6-$[CH_2P(i\text{-}Pr)_2]_2Pd(TFA)\}$ (TFA = trifluoroacetate),[5] $[(C_5H_3N$-2,6-$(NHC^{Me})Pd(Br)]^+$,[6c] $[(C_6H_4$-2-$(CH_2P(t\text{-}Bu)_2)Pd(OAc)]_2$,[27] $[(C_6H_2$-3,5-$(t\text{-}Bu)_2$-2-$\{OP(OAr)_2\}Pd(Cl)]_2$[28] or the palladium phosphinito PCP pincer complex ($\{C_6H_3$-2,6-$[OP(i\text{Pr})_2]_2\}Pd(Cl)$).[6o] Complex **1** is even more active than the very recently reported systems like $[(C^{NHC}N)Pd(fppz)]$ (fppzH = 2-[3-(trifluoromethyl)-1*H*-pyrazol-5-yl]pyridine) and *trans*-di(μ-aceto)bis[2-diphenylphospino-2′-methylbiphenyl]dipalladium.[29,30] On the other hand, the recently published aminophosphine-based pincer complex $[C_6H_3$-2,6-$\{NHP(piperidinyl)_2\}_2Pd(Cl)]$ shows a higher performance when sterically hindered aryl bromides were used as substrates.[7b] In contrast, **1** is more efficient when electronically deactivated aryl bromides (4-bromoanisole, e.g.) were applied or 4-vinylpyridine was used as coupling partner. However, apart from comparisons with literature data, which already indicated an improved catalytic activity and functional group tolerance of the aminophosphine-based system when compared to the above mentioned catalysts, a comparative study with **1**, $[Pd(OAc)_2]$ and $[(C_6H_4$-2-$(CH_2P(t\text{-}Bu)_2)Pd(OAc)]_2$ was performed with a series of randomly chosen aryl bromides and olefins at 140 °C in DMF and K_3CO_3 as solvent and base in the presence of 0.05 mol% (relative to palladium) of catalyst. Indeed, this study impressively demonstrated that the aminophosphine-based catalyst is superior to palladium acetate and Herrmann's system – at least under the reaction conditions applied. Whereas almost complete product formations for the cross-coupling of 1-bromo-4-methoxybenzene with styrene, and 4-bromobenzonitrile, 3-bromobenzaldehyde or 1-bromonaphthalene with butyl prop-2-enoate were found for all examined catalysts, a significantly higher catalytic activity of **1** when compared to $[Pd(OAc)_2]$ was generally noticed when sterically hindered aryl bromides were applied: for example, while conversions of >90% into the respective coupling products were achieved with **1** and ($\{C_6H_4$-2-$[CH_2P(t\text{-}Bu)_2]Pd(OAc)\}_2$) when 1-bromo-2-methylbenzene or 2-bromo-1,3,5-trimethylbenzene were coupled with styrene, only 64 and 6% conversion into 1-methyl-2-[(*E*)-2-phenylethenyl]benzene and 1,3,5-trimethyl-2-[(*E*)-2-phenylethenyl]benzene, respectively, was noticed when palladium acetate was applied. On the other hand, whereas an almost quantitative conversion of ethyl 4-bromobenzoate into ethyl 4-[(*E*)-2-

phenylethenyl]benzoate was achieved with $[Pd(OAc)_2]$ and the aminophosphine-based palladium system, only 66% of the coupling product was formed when Herrmann's system was used as catalyst. Similarly, while complete C–C bond formations were achieved with palladium acetate and **1** when 6-bromo-*N*-ethyl-*N*-phenylpyridin-2-amine was coupled with 4-vinylpyridine, 81% conversion into *N*-ethyl-*N*-phenyl-6-[(*E*)-2-pyridin-4-ylethenyl]pyridin-2-amine was obtained with $(\{C_6H_4\text{-}2\text{-}[CH_2P(t\text{-}Bu)_2]\}Pd(OAc)]_2)$. Moreover, a significantly improved catalytic activity was found for **1** when compared to both, $[Pd(OAc)_2]$ and $(\{C_6H_4\text{-}2\text{-}[CH_2P(t\text{-}Bu)_2]\}Pd(OAc)]_2)$, when 5-bromo-2-benzofuran-1(3*H*)-one or heterocyclic substrates, such as 2-bromothiophene or 3-bromoquinoline were coupled with styrene: while the coupling products were almost quantitatively formed with **1**, conversions between 50 and 75% have been obtained when palladium acetate or Herrmann's system were applied. Overall, the comparative study clearly demonstrated that the aminophosphine-based palladium complex **1** is indeed superior to both, palladium acetate and Herrmann's system – under the reaction conditions applied. In addition to the improved catalytic activity of **1** in the Heck cross-coupling reaction further, great advantages when compared to palladium acetate and Herrmann's system were noticed: **1** exhibit an excellent functional group tolerance and hence, shows in contrast to $Pd(OAc)_2]$ and $(\{C_6H_4\text{-}2\text{-}[CH_2P(t\text{-}Bu)_2]\}Pd(OAc)]_2)$ a consistently high catalytic activity with all the aryl bromides tested, allowing the conversion rates and yields of coupling reactions with other substrates to be much better predicted than it is the case for palladium acetate and Herrmann's system. Finally it may be mentioned that comparisons with $[Pd_2(dba)_3]/P(t\text{-}Bu)_3$ (dba = dibenzylideneacetone). for example, are not possible, as the Heck reactions are typically performed with aryl chlorides.[31]

Apart from the excellent catalytic activity and functional group tolerance of dichlorobis[1-(dicyclohexylphosphanyl)piperidine]palladium (**1**) in the Heck reaction, a further advantage of **1** (or aminophosphine-based systems in general) when compared to water-insoluble phosphine-based ligand systems includes their sensitivity towards protons: It was recently demonstrated that dichloro{bis[1-(dicyclohexylphosphanyl)-piperidine]}palladium (**1**) degrades in the presence of water in air at elevated temperatures into dicyclohexylphosphinate and other, insoluble, palladium-containing products.[11a] In a similar way, treatment of **1** with aqueous hydrochloric acid in air and thus, under work-up conditions led to a rapid catalyst degradation and the formation of products which are easily separated from the coupling products – an often ignored but very important issue for the preparation of pharmaceutically active compounds, e.g.

Mechanistic Investigations

Although detailed mechanistic investigations have not been performed, the following experimental observations clearly indicate the involvement of palladium nanoparticles in the catalytic cycle of the Heck reaction. (i) Sigmoidal-shaped kinetics with induction periods (typically between 10 and 20 min) were observed in all the coupling reactions examined (Figure 1).[32] (ii) The addition of water to reaction mixtures of aryl bromide, olefin and catalyst led to decreased induction periods (due to faster catalyst degradation and thus,[33] faster palladium nanoparticle formation) but was often found to be accompanied by lowered product yields – most probably due to the formation of inactive palladium black.[34] (iii) The addition of a large excess of metallic mercury to reaction mixtures of aryl bromide, olefin and catalyst efficiently stopped catalysis and no product formation at all was observed when Hg(0) was added at the beginning of the reaction.[35] Essentially the same observations were made when poly(4-vinylpyridine) (PVPy) (2% cross-linked with divinylbenzene) was used instead.[36] (iv) No product formation at all was obtained when 0.1 equiv. (relative to catalyst) of CS_2 was present in the reaction mixtures. (v) Neither the conversion rates nor the product yields were affected by the presence of about 20 mol% (relative to aryl bromide) of NBu_4Br.[38] (vi) Catalyst concentrations >0.1 mol% are not appropriate and lead to the fast deposition of inactive palladium black. (vii) Whereas comparable catalytic activities were observed for **1** and dichloro{bis[1,1′,1″-(phosphanetriyl)tripiperidine]}palladium (**2**), a reduced catalytic activity was noticed for dichlorobis[1,1′-(cyclohexylphosphanediyl)dipiperidine]palladium (**3**). A significant drop in activity was found for their phosphine-based analogue $[(P(C_6H_{11})_3)_2Pd(Cl)_2]$ (**4**), the most stable system of this series – another piece of evidence that dichloro-{bis[1-(dicyclohexylphosphanyl)piperidine]}palladium (**1**) is a pre-catalyst that is transformed into palladium nanoparticles.[39] Indeed, their presence could be verified by analysis of the reaction mixture by a transmission electron microscopy (TEM) equipped with an energy dispersive X-ray (EDX) analysator (Figure 2).

Conclusions

In conclusion, complex **1** is an extremely efficient, versatile and reliable Heck catalyst with an excellent functional group tolerance, which enables us to selectively and quantitatively couple a large variety of electronically activated, non-activated, deactivated and/or sterically hindered aryl bromides, which may contain nitro, chloro or trifluoromethane groups, nitriles, acetales, ketones, aldehydes, ethers, esters, lac-

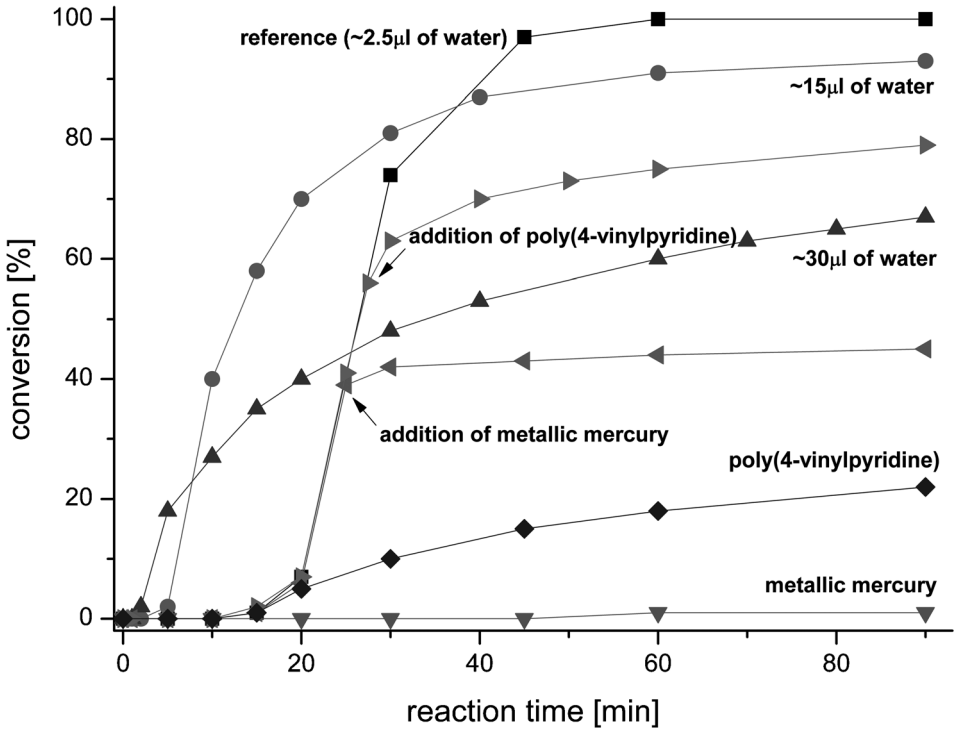


Figure 1. Kinetics of the Heck reaction of 1-bromo-4-methoxybenzene with styrene in the presence and in the absence of additives, catalyzed by 0.05 mol% of dichloro{bis[1-(dicyclohexylphosphanyl)piperidine]}palladium (**1**) at 140 °C in DMF.

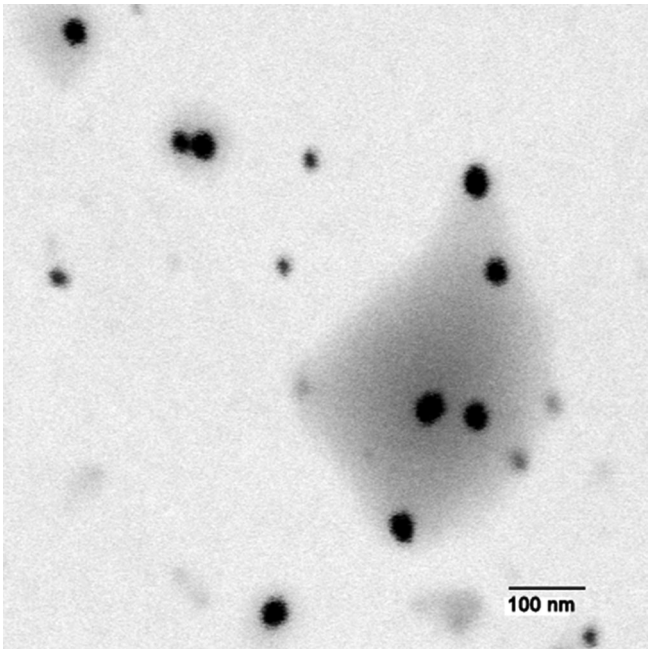


Figure 2. TEM image showing palladium nanoparticles (as indicated by EDX analysis) from the cross-coupling reaction of 1-bromo-4-methoxybenzene with styrene, catalyzed by 0.05 mol% of dichloro{bis[1-(dicyclohexylphosphanyl)piperidine]}palladium (**1**) at 140 °C in DMF.

tones, amides, anilines, phenols, alcohols, carboxylic acids, as well as heterocyclic aryl bromides, such as pyridines and derivatives, or thiophenes and aryl bromides with methylsulfanyl groups that have been successfully coupled with various olefins under uniform reaction conditions, generally within only few hours of reaction time in DMF and K_2CO_3 as solvent and base at 140 °C in the presence of only 0.05 mol% of catalyst. Even though catalyst loadings between 0.002 and 0.01 mol% would be sufficient to achieve similar conversions for many of the substrates tested, the great advantage of the reaction protocol described here lies in its general applicability, which allows a direct adoption to other aryl bromides without the neccessity of its modification. Overall, the demonstration of such a broad applicability in the Heck reaction of a single catalyst under uniform reaction conditions is unprecedented. Moreover, the coupling products of all the reactions examined were cleanly formed and hence, could have been isolated in good to excellent yields. All the experimental observations indicate that palladium nanoparticles are the catalytically active form of the dichloro-bis(aminophosphine) complexes **1–3** and thus, provide a simple explanation why aminophosphine-based complexes of palladium are superior to their phosphine-based systems when aryl bromides are used as substrates.

Experimental Section

General

All synthetic operations for the catalyst preparation were carried out in oven-dried glassware using a combination of glovebox (M. Braun 150B-G-II) and Schlenk techniques under a dinitrogen atmosphere. Solvents were reagent grade or better and freshly distilled under N_2 atmosphere by standard procedures. All chemicals were purchased from Aldrich Chemical Co. and used as received.

Analysis

^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR data were recorded at 500.13, 125.76 and 202.46 MHz, respectively, on a Bruker DRX-500 spectrometer or at 300.1, 121.5 and 75.4 MHz, respectively, on a Varian Gemini spectrometer. Chemical shifts (δ) are expressed in parts per million (ppm), coupling constants (*J*) are in Hz. The ^1H and ^{13}C NMR chemical shifts are reported relative to tetramethylsilane; the resonance of the residual protons of the solvent was used as internal standard for ^1H ($\delta = 7.15$ benzene, 5.32 dichloromethane) and all deuterium solvent peaks for ^{13}C ($\delta = 128.0$ benzene, 53.8 dichloromethane). All measurements were carried out at 298 K. Abbreviations used in the description of NMR data are as follows: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad. Elemental analyses were performed on a Leco CHNS-932 analysator at the University of Zürich, Switzerland. TEM-EDX analysis was performed on a Tecnai G2 Spirit 120 kV (FEI, Eindhoven, Netherlands) using an Oxford X-Max 80 EDX Detector (Oxford Instruments, Oxfordshire, UK) at the center for microscopy and image analysis at the University of Zürich, Switzerland

Preparation of ($\{P[(NC_5H_{10})(C_6H_{11})_2]_2\}Pd(Cl)_2$) (1)[11a]

100 mg (0.35 mmol) of $[Pd(cod)(Cl)_2]$ were suspended with 10 mL of toluene. After the addition of toluene solutions (10 mL) containing two equivalents of $P(NC_5H_{10})(C_6H_{11})_2$, the reaction mixture was stirred for 10 min. Removal of the volatiles under reduced pressure and the addition of pentane, followed by filtration afforded the yellow, analytically pure palladium complex **1** in almost quantitative yield. $^{31}P\{^1H\}$ NMR (C_6D_6): δ = 80.0 [s, $P((NC_5H_{10})(C_6H_{11})_2]$; ^1H NMR (C_6D_6): δ = 3.21 (broad s, 8H), 3.62 (broad s, 4H), 3.32–2.28 (m, 4H), 1.95–1.16 (m, 48H); $^{13}C\{^1H\}$ NMR (C_6D_6): δ = 51.8 (t, $J = 49.5$ Hz), 35.9 (t, $J = 50.3$ Hz), 30.4, 28.6, 27.5–27.2 (overlapping signals), 25.0.

Preparation of *cis*-$[(P\{(NC_5H_{10})_n(C_6H_{11})_{3-n}\})(NC_5H_{10})Mo(CO)_4]$ (1–3)

200 mg (0.52 mmol) of $[Mo(CO)_4(NC_5H_{10})_2]_2$ were suspended in 5 mL of CH_2Cl_2. After the addition of an equimolar amount of appropriate ligand (dissolved in CH_2Cl_2), the reaction mixture was stirred for 15 min at 50 °C. Removal of the volatiles under reduced pressure and the addition of pentane, followed by filtration afforded the pale yellow, analytically pure molybdenum complexes **1–3** in almost quantitative yields.

Data for 1: $^{31}P\{^1H\}$ NMR (CD_2Cl_2): δ = 140.6 [s, $P(NC_5H_{10})_3$]; ^1H NMR (CD_2Cl_2): δ = 8.74 (br s, 1H) 3.29–2.75 (m, 16H), 1.98–1.29 (m, 24H); $^{13}C\{^1H\}$ NMR (CD_2Cl_2): δ = 219.0 (d, $^3J_{P,C} = 10.5$ Hz), 215.9 (d, $^1J_{P,C} = 41.0$ Hz), 209.5 (d, $^2J_{P,C} = 10.9$ Hz), 56.9, 47.2 (overlapping signals), 28.3, 26.8 (overlapping signals), 25.4, 23.1; IR (ATR): $A1_{\nu(CO)} = 2007$ cm^{-1}; elemental analysis: calcd. for $C_{27}H_{40}MoN_4O_4P$: C 50.09, H 7.01, N 9.74; found: C 49.92, H 6.99, N 9.69.

Data for 2: $^{31}P\{^1H\}$ NMR (CD_2Cl_2): δ = 131.2 [s, $P(NC_5H_{10})_2(C_6H_{11})$]; ^1H NMR (CD_2Cl_2): δ = 9.01 (br s, 1H), 3.33–2.79 (m, 12H), 2.46–1.38 (m, 29H); $^{13}C\{^1H\}$ NMR (CD_2Cl_2): δ = 219.3 (d, $^3J_{P,C} = 8.7$ Hz), 216.7 (d, $^1J_{P,C} = 37.6$ Hz), 210.7 (d, $^2J_{P,C} = 9.7$ Hz), 57.0, 50.3, 35.7 (d, $J = 29.2$ Hz), 28.6, 27.6 (overlapping signals), 27.1 (overlapping signals), 26.4, 25.4, 23.5; IR (ATR): $A1_{\nu(CO)} = 2006$ cm^{-1}; elemental analysis: calcd. for $C_{25}H_{41}MoN_3O_4P$: C 52.26, H 7.19, N 7.31; found: C 52.42, H 7.39, N, 7.51.

Data for 3: $^{31}P\{^1H\}$ NMR (CD_2Cl_2): δ = 105.3 [s, $P((NC_5H_{10})(C_6H_{11})_2]$; ^1H NMR (CD_2Cl_2): δ = 8.79 (broad s, 1H), 3.20–2.79 (m, 8H), 2.02–0.89 (m, 34H); $^{13}C\{^1H\}$ NMR (CD_2Cl_2): δ = 219.6 (d, $^3J_{P,C} = 7.4$ Hz), 216.1 (d, $^1J_{P,C} = 33.8$ Hz), 210.8 (d, $^2J_{P,C} = 8.7$ Hz), 57.3, 51.8, 39.1 (d, $J = 14.0$ Hz), 28.6 (overlapping signals), 27.7 (overlapping signals), 26.8, 25.5, 23.4; IR (ATR): $A1_{\nu(CO)} = 2006$ cm^{-1}; elemental analysis: calcd. for $C_{26}H_{42}MoN_2O_4P$: C 54.45, H 7.38, N 4.88; found: C 54.19, H 7.30, N 4.79.

Data for 4: IR (ATR): $A1_{\nu(CO)} = 2005$ cm^{-1}.[42]

General Procedure for Heck Cross-Coupling Reactions

A round-bottomed flask was charged under N_2 with the appropriate olefin (1.5 mmol), aryl bromide (1.0 mmol), powdered K_2CO_3 [347825; potassium carbonate – reagent grade, ≥98%, powder, −325 mesh (Sigma–Aldrich), 2.0 mmol], and 2.5 mL of DMF [33120; *N,N*-dimethylformamide – puriss. p. a., ACS reagent, reag. Ph. Eur., ≥99.8% (GC) (Sigma–Aldrich)]. The mixture was vigorously stirred and heated to 140 °C. Then the catalyst was added by syringe as a solution (0.05 mol%, 0.1 mL of a 5×10^{-3} M THF solution). Samples were periodically taken from the reaction mixture, quenched with 1 M aqueous HCl (or 1 M NaOH when basic functional groups are present), extracted with ethyl acetate, and analyzed by GC/MS. At the end of catalysis, the reaction mixtures were allowed to cool to room temperature, quenched with 1 M aqueous HCl (or 1 M NaOH when basic functional groups are present in the coupling products), and extracted with ethyl acetate (3 × 25 mL). The combined extracts were dried ($MgSO_4$) and evaporated to dryness. The crude material was purified by flash chromatography on silica gel, as necessary.

Acknowledgements

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