Palladacycles: Efficient New Catalysts for the Heck Vinylation of Aryl Halides**

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Abstract: Cyclopalladated complexes of the general formula $[Pd_2(\mu\text{-}L)_2(P\text{-}C)_2]$ (L = bridging ligand, e.g. OAc, Cl, Br, I; P–C = cyclometallated P donor, e.g. *o*-$CH_2C_6H_4P(o\text{-}Tol)_2$ or *o*-$CH_2C_6H_2(CH_3)_2$-$P(Mes)_2$) are highly efficient catalysts for the Heck vinylation of aryl halides. The isolated complexes are easily accessible from palladium(II) acetate by spontaneous metallation of *ortho*-methyl-substituted arylphosphines. They display improved activity and stability compared to conventional catalyst mixtures (e.g. $[Pd(OAc)_2] + n PPh_3$), and also exhibit a higher stability towards air than conventional Pd^0-based systems (e.g. $[Pd(PPh_3)_4]$). Turnover numbers (TON) of up to 1 000 000 and turnover frequencies (TOF) in the range of 5000–20 000 are achieved in catalytic coupling reactions of aryl bromides. Even technically interesting aryl chlorides undergo the Heck reaction (TON = 600–40 000) if promoting salts are added to the catalyst ($(NBu_4)Br$, LiBr). The new structural type for catalysts is compared to palladacycles formed in situ from mixtures of $[Pd(OAc)_2] + P(o\text{-tolyl})_3$ and the established $[Pd(OAc)_2] + n PPh_3$ system. The scope of the new C–C coupling catalysts is outlined for the vinylation of aryl halides by the use of different mono- and disubstituted olefins. Mechanistic consequences for the Heck reaction in general are discussed.

Keywords
aryl halides · catalysis · Heck reaction · metallacycles · palladium

Introduction

The palladium-catalyzed arylation of olefins with aryl halides — generally referred to as the Heck reaction[1]—has received increasing attention in the last decade. This is primarily due to the enormous synthetic potential of this versatile method for generating new carbon–carbon bonds.[2] However, the reaction suffers from severe limitations which have so far precluded widespread industrial applications.[3] Typically, a relatively large amount of catalyst (1–5 mol%) is needed for reasonable conversions and catalyst recycling is often hampered by early precipitation of palladium black.[2a, b] Another drawback is the failure of the industrially attractive aryl chlorides to undergo Heck reactions with reasonable catalyst activities.

Only a few approaches towards catalyst improvement, such as the use of highly basic and sterically hindered phosphines,[4, 5] the use of a large excess of coordinating ligands (e.g. triphenylphosphine[6]) or the application of high pressure conditions[7] have been described.

Active catalyst systems have been obtained by using palladacycles formed in situ from mixtures of Pd^{II} salts and tris-*o*-tolylphosphine.[8] We have recently shown that these catalyst mixtures primarily react to form palladacycles under the conditions of the Heck reaction.[9] In contrast, $Pd^{II}/P(C_6H_5)_3$ catalysts suffer from phosphine degradation due to aryl scrambling.[10] In the following, we report outstanding catalyst activities for the reaction of aryl halides with alkyl acrylates, styrene, and alkyl enol ethers by the use of cyclometallated palladium(II)-phosphine complexes.

Results and Discussion

Preparation of the catalysts: When palladium(II) acetate is treated with the sterically demanding triarylphosphines $P(o\text{-Tol})_3$ and $P(Mes)_3$ in toluene, the yellow complexes **1a** and **2a** are formed in high yields (90–95%). These cyclometallated compounds are stable solids and result from simple C–H activation of one *ortho*-methyl group in the phosphine and concomitant elimination of acetic acid (Scheme 1).

Complexes **1a** and **2a** are fluxional molecules in solution, as evidenced by broad $^{31}P\{^1H\}$ NMR resonances at room temperature. This non-rigidity is primarily due to the weakly bound acetate ligands, which give rise to monomer/dimer equilibria in solution. Coordinating solvents participate in these equilibrations, favoring bridge-splitting of the complexes (^{31}P and ^1H NMR studies).[10b, 11] Cooling to −40 °C slows the dynam-

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[**] Coordination chemistry and mechanisms of metal-catalyzed C–C coupling reactions, Part 10; for Part 9, see ref. [24].

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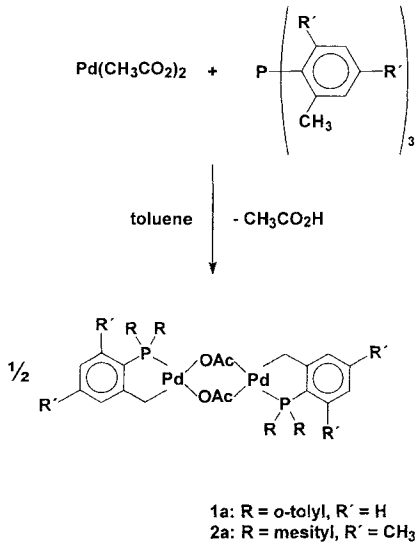


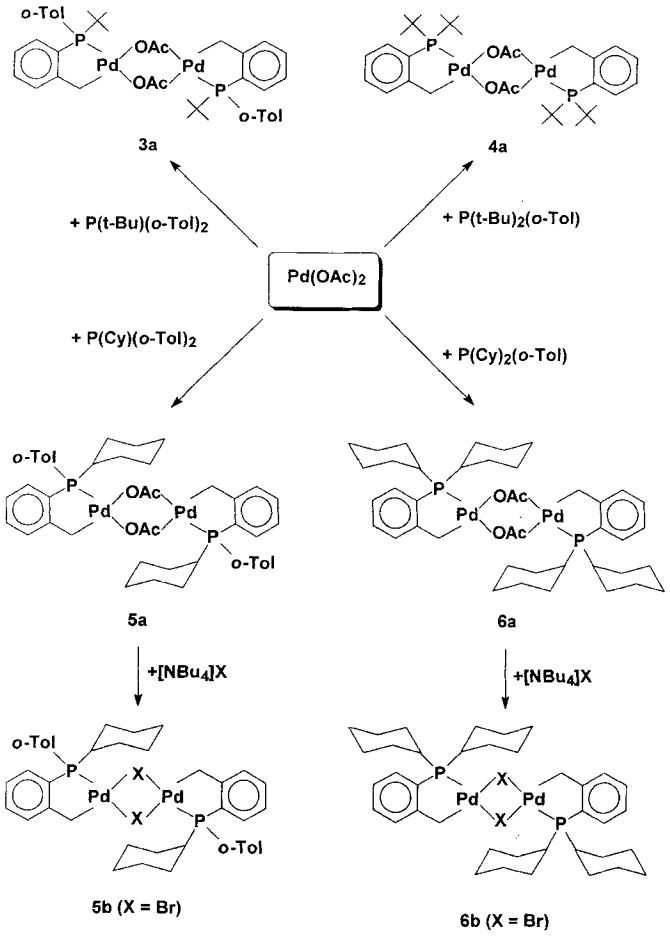
Scheme 1. Synthesis of palladacycles by the direct metallation of P(*o*-Tol)$_3$ and P(Mes)$_3$.

ics to such an extent that sharp singlets are detected for **1a** and **2a** in the $^{31}P\{^1H\}$ NMR spectrum.

The labile acetate groups in **1a** and **2a** are easily exchanged by halogen ligands X (Cl, Br, I) by a metathesis reaction with tetrabutylammonium salts. The resulting halogen-bridged complexes, **1b** and **2b** respectively, are also very stable,[12] but show inferior solubility in noncoordinating solvents (CH_2Cl_2, toluene). Addition of either strongly coordinating solvents (DMSO, DMF, CH_3CN) or donor ligands (PPh_3, pyridine, NEt_3) results in bridge-splitting and formation of more soluble mononuclear products. The presence of an excess of halide ions has the same effect and leads to mononuclear anionic complexes.

The cyclometallated Pd^{II} complexes exhibit high thermal stability in the solid state. According to TG/MS measurements, **1a** does not decompose until 250 °C, which is about 100 °C above the decomposition temperature of conventional Pd^{II} complexes (e.g. *trans*-$[Pd(PPh_3)_2(OAc)_2]$ or $[Pd_2(PPh_3)_2(\mu\text{-}OAc)_2(OAc)_2]$).

Other *ortho*-tolylphosphines besides P(*o*-Tol)$_3$ and P(Mes)$_3$ are equally well cyclometallated by palladium acetate if sterically demanding groups are attached to the phosphorus atom. Particularly *t*-butyl-[11] and cyclohexyl-substituted *o*-tolylphosphines have proved to be favorable candidates for cyclometallation. A variety of alkyl-substituted palladacycles (**3a**–**6b**), accessible by direct metallation of $[Pd(OAc)_2]$, are presented in Scheme 2. In contrast to **1** and **2**, these analogues exhibit *two* singlets in the $^{31}P\{^1H\}$ NMR spectrum at low temperature (−70 °C), which can be assigned to the *cis*- and *trans*-configured isomers. The latter rapidly equilibrate via mononuclear intermediates at ambient temperature.



Scheme 2. Alkyl-substituted palladacycles **3a**–**6b**.

Catalysis: Cinnamic ester derivatives are an interesting class of compounds because they are used industrially as UV absorbers, as antioxidants in plastics, and as intermediates for pharmaceuticals.[13] Thus, we initially investigated the reaction of various aryl bromides with *n*-butyl acrylate. C–C coupling in the presence of sodium acetate and catalytic amounts of **1a** leads quantitatively, or in very good yields (>90%), to the corresponding *n*-butyl cinnamates. Table 1 summarizes the results of the catalyzed reactions.

An extraordinarily high reactivity has been observed for activated aryl bromides (e.g. 4-bromobenzaldehyde and 4-bromoacetophenone). Extremely low catalyst concentrations (ca. 1×10^{-4} mol%) are fully sufficient. Consequently, turnover numbers (TON) as high as 1000000 [mol product/mol palladium] have been achieved for the first time, albeit with electron-poor aryl bromides. Compared with the best TON from the literature (TON: 134000, in situ catalyst: $[Pd(OAc)_2]$/4P(*o*-tolyl)$_3$) our results are about one order of magnitude better.[8] Turnover frequencies (TOF) generally range between 5000 and 50000 [mol product mol palladium^{-1} h^{-1}] (see Table 1). Electron-rich aryl bromides (e.g. 4-bromoanisole, 2-bromotoluene) with rather diminished reactivity require higher catalyst concentrations (0.5–1 mmol **1a**) and longer reaction times. Nevertheless, these are the highest turnover numbers ever achieved for deactivated aryl bromides.

Next, different palladacycles were compared in the standard reaction of 4-bromobenzaldehyde with *n*-butyl acrylate. The reaction profiles given in Figure 1 clearly show that catalysts containing aryl groups (*o*-tolyl, mesityl) bound to phosphorus are superior to those containing the bulky *t*-butyl groups. The higher rates found for **1a** and **2b** in comparison to **3a** and **4a** may be rationalized on the basis of differing basicities of the respective P atoms; however, steric effects of the substituents

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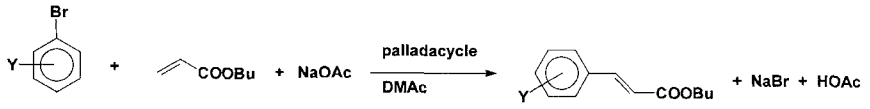
Table 1. Heck olefination of aryl bromides with *n*-butyl acrylate and palladacycles **1a** and **2b** as catalysts (Y = H, 4-CHO, 4-CN, 4-$COCH_3$, 2-CH_3, 4-OCH_3).



No.	Aryl halide	Catalyst (mol% Pd)	Additive/promotor (mol%)	T (°C)	Reaction time (h)	Conversion [%] [a]	Yield (%) [b]	TON (mol product/mol Pd)
1	4-bromobenzaldehyde	**1a** (1)	–	100	2	>99	>99	100
2	4-bromobenzaldehyde	**1a** (0.01)	–	130	3	>99	>99	10000
3	4-bromobenzaldehyde	**1a** (0.001)	–	135	12	>99	>99	100000
4	4-bromobenzaldehyde	**2b** (0.01)		130	2	>99	>99	10000
5	4-bromoacetophenone	**1a** (0.0001)	NBu_4Br (20)	130	24	>99	>99	1000000
6	4-bromoacetophenone	**Pd(OAc)$_2$** (0.0001)	PPh_3 (0.0002) NBu_4Br (20)	130	24	>99	>99	1000000
7	4-bromoacetophenone	**Pd(OAc)$_2$** (0.0001)	P(*o*-Tol)$_3$ (0.0002) NBu_4Br (20)	130	24	>99	>99	1000000
8	4-bromoacetophenone	**2b** (0.001)	–	135	10	>99	>99	100000
9	4-bromobenzonitrile	**1a** (0.02)		135	1	>99	>99	5000
10	bromobenzene	**1a** (2)	–	140	48	>99	96	48
11	2-bromotoluene	**1a** (2)	–	140	48	>99	92	46
12	4-bromoanisole	**1a** (2)	–	140	48	>99	94	47
13	4-bromoanisole	**Pd(OAc)$_2$** (1)	P(*o*-Tol)$_3$ (1)	140	93	84	75	75
14	4-bromoanisole	**1a** (1)	–	140	48	93	87	87
15	4-bromoanisole	**2b** (2)	–	138	44	85	74	37

[a] GLC-conversion of the corresponding aryl halide. [b] GLC-yield of the corresponding Heck coupling product with reference to aryl halide.

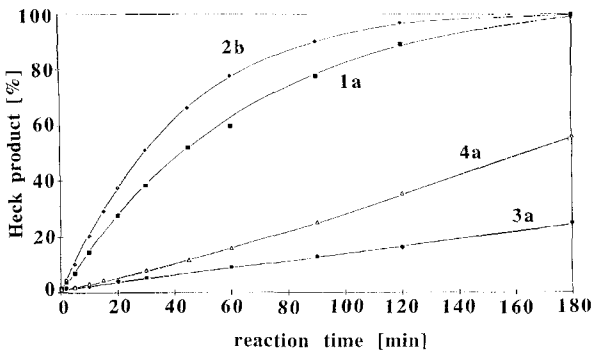


Figure 1. Comparison of different palladacycles in the Heck reaction: concentration against time for the formation of *n*-butyl (*E*)-4-formylcinnamate (GLC). Reaction conditions: 4-bromobenzaldehyde (100 mmol), *n*-butyl acrylate (150 mmol), anhydrous sodium acetate (110 mmol), *N*,*N*-dimethylacetamide (100 mL), GLC standard (2 g); T = 130 °C; catalysts: 0.005 mmole of the palladacycles **1a** ■, **2b** ◆, **3a** ●, and **4a** △ (0.01 mol% Pd).

should also be considered. The mesityl complex **2b** shows a slightly higher activity than the *o*-tolyl compound **1a** (inductive and steric effects of the methyl groups in the *ortho*- and *para*-positions). In contrast, the influence of the bridging ligand—OAc versus Br—seems to be of minor importance.

The mechanism of the Heck reaction in the presence of palladacycles has not yet been fully established. It is known that the Pd^{II} salts employed in catalysis are reduced by added organophosphine ligands to yield catalytically active *zerovalent* palladium–phosphine complexes.[14] The latter activate haloarenes by oxidative addition with the formation of arylpalladium(II) halide species.[15] In the case of our palladacycles (Pd^{II}) no evidence for a reduction under Heck reaction conditions was observed. Neither in situ NMR spectroscopy nor isolation of the palladacycle after successful catalysis, albeit not in quantitative yield, indicate the formation of $[Pd\{P(o\text{-}Tol)_3\}_2]$. Other mechanisms thus have to be taken into consideration. In this respect, a process without a redox change or a $Pd^{II} \rightarrow Pd^{IV}$ step cannot be ruled out.[16] Unfortunately, all attempts to isolate an arylpalladium(IV) complex failed. It seems that **1a** does not react with the aryl bromide *until the olefin is added to the mixture*. Detailed spectroscopic studies (in situ ^{31}P NMR) revealed that the acetate-bridged complex **1a** develops its catalytic activity for 4-bromobenzaldehyde and *n*-butyl acrylate at about 80 °C. An acetate/bromide exchange occurs in the early stages of the Heck reaction. The palladacycle **1a** disappears with increasing conversion and, consequently, with higher bromide concentration. At the end of the reaction, only the anionic complex $[Pd(o\text{-}CH_2C_6H_4P(o\text{-}Tol)_2)Br_2]^-$ (**1b′**) remains in solution (from 10–100% conversion). Other intermediates observed in the ^{31}P NMR experiment are the solvent-coordinated mononuclear, neutral species $[Pd(o\text{-}CH_2C_6H_4P(o\text{-}Tol)_2)(DMF)Br]^0$ (**1b″**) and the halogen-bridged dinuclear species $[(Pd(o\text{-}CH_2C_6H_4P(o\text{-}Tol)_2)Br)_2]$ (**1b**). After complete conversion, the anionic complex **1b′** was isolated in the form of the bromo-bridged derivative **1b**, which readily crystallized from the cooled reaction mixture. An almost quantitative yield (90%) of **1b** was obtained after removal of the solvent and addition of diethyl ether or *n*-hexane to the organic residue. However, a Pd^0–phosphine species in a very low concentration cannot be excluded as the active catalyst, although no such species is observed in the NMR experiment. In subsequent catalytic runs the recycled palladacycle **1b** can be used as the catalyst instead of **1a** (see Figure 1). Activation or functionalization of the mononuclear palladacycles with the incoming substrates (olefin, aryl bromide) is very fast at 80 °C, and could not be monitored spectroscopically.

In order to study the effect of the olefin in Heck reactions, the reaction of aryl bromides with styrene, butyl vinyl ether and the disubstituted olefin 1-methylstyrene were investigated in the presence of the palladacycle **1a** as the catalyst. The results are summarized in Table 2. Styrene gave excellent TONs, similar to *n*-butyl acrylate. Compared to previous data (TON: 65000, in

Table 2. Heck olefination of aryl bromides with various olefins and palladacycle **1a** as catalyst.

No.	Olefin	Aryl halide	Catalyst (mol% Pd)	Additive/ promotor (mol%)	Reaction time (h)	Product(s) (yield[%])	TON (mol product/mol Pd)
1	styrene	4-bromoacetophenone	**1a** (0.1)	–	24	(*E*)-4-acetylstilbene (89) [a]	890
2	styrene	4-bromoacetophenone	**1a** (0.0001)	–	72	(*E*)-4-acetylstilbene (49) [a]	490000
3	styrene	4-bromoacetophenone	**$Pd(OAc)_2$** (0.0001)	–	72	(*E*)-4-acetylstilbene (56) [a]	560000
4	styrene	4-bromoacetophenone	**$Pd(OAc)_2$** (0.0001)	PPh_3 (0.0002)	72	(*E*)-4-acetylstilbene (94) [a]	940000
5	styrene	4-bromofluorobenzene	**1a** (0.1)	–	25	(*E*)-4-fluorostilbene (93) [a]	930
6	styrene	4-bromofluorobenzene	**1a** (0.0001)	–	72	(*E*)-4-fluorostilbene (36) [a]	360000
7	styrene	4-bromochlorobenzene	**1a** (0.0001)	–	72	(*E*)-4-chlorostilbene (41) [a]	410000
8	styrene	bromobenzene	**1a** (0.1)	–	26	(*E*)-stilbene (77) [a]	770
9	styrene	bromobenzene	**1a** (0.0001)	–	72	(*E*)-stilbene (29) [a]	290000
10	styrene	3-bromotoluene	**1a** (0.1)	–	30	(*E*)-3-methylstilbene (62) [b]	620
11	styrene	4-bromoanisole	**1a** (0.1)	–	30	(*E*)-4-methoxystilbene (69) [a]	690
12	styrene	4-bromoanisole	**1a** (0.0001)	–	72	(*E*)-4-methoxystilbene (22) [a]	220000
13	styrene	4-bromoanisole	**$Pd(OAc)_2$** (0.0001)	PPh_3 (0.0002)	72	(*E*)-4-methoxystilbene (16) [a]	160000
14	4-fluorostyrene	4-bromoanisole	**1a** (0.1)	–	30	(*E*)-4-fluoro-4′-methoxystilbene (85) [a]	850
15	4-methoxystyrene	4-bromoanisole	**1a** (0.1)	–	30	(*E*)-4,4′-bismethoxystilbene (30) [a]	300
16	1-methylstyrene	4-bromochlorobenzene	**1a** (0.1)	–	24	1-(4-chlorophenyl)-2-phenyl-1-propene (10) [b,c] 2-phenyl-3-(4-chlorophenyl)-1-propene (27) [b,c] double arylated product (13) [b,c]	630
17	*n*-butyl vinyl ether	4-bromoacetophenone	**1a** (0.1)	$[NBu_4]Br$ (20)	5	(*E*)-(2-butoxyethenyl)-4-acetylbenzene (52) [d] (*Z*)-(2-butoxyethenyl)-4-acetylbenzene (29) [d] (1-butoxyethenyl)-4-acetylbenzene (16) [d]	970
18		bromobenzene	**1a** (0.1)	$[NBu_4]Br$ (20)	24	(*E*)-(2-butoxyethenyl)benzene (44) [d] (*Z*)-(2-butoxyethenyl)benzene (23) [d] (1-butoxyethenyl)benzene (19) [d]	860
19		4-bromoanisole	**1a** (0.1)	$[NBu_4]Br$ (20)	24	(*E*)-(2-butoxyethenyl)-4-methoxybenzene (16) [d] (*Z*)-(2-butoxyethenyl)-4-methoxybenzene (19) [d] (1-butoxyethenyl)-4-methoxybenzene (28) [d]	540

[a] Isolated by crystallization. [b] Isolated by column chromatography. [c] Ratio of the isomers determined by ^1H NMR. [d] GLC yield.

situ catalyst: $[Pd(OAc)_2]/4P(o\text{-tolyl})_3$) for coupling reactions with styrene, again, our data are about one order of magnitude higher, up to a TON of 1 000 000.[8] The catalytic activity was significantly lower for the electron-rich butyl vinyl ether; nevertheless, TONs up to 1000 have been achieved here for the first time.

It is obvious from Table 2 that both the electronic nature of the olefin and steric hindrance are decisive factors for the efficiency of the catalysts. The influence of electronic factors is seen from reactions of 4-substituted styrenes (runs 11, 14 and 15, Table 2). Here, electron-withdrawing groups *increase* the yield of the corresponding stilbene, and vice versa. With 1-methylstyrene as an example of a 1,1-disubstituted olefin, it became evident that the palladacycle catalyst is rather sensitive towards steric hindrance. Nevertheless, the TON data are one order of magnitude higher compared to any previous report for this olefin (TON: 86, catalyst: $[Pd(OAc)_2]/2P(Ph)_3$).[19]

This result suggests that the rate-determining step in the Heck reaction of aryl bromides is *not* the oxidative addition of the actual palladium catalyst, but rather the insertion of the olefin into the arylpalladium intermediate.[14c] This assumption is further supported by the competitive reaction of styrene and *n*-butyl acrylate with 4-bromoacetophenone, which led to a mixture of 14% 4-acetylstilbene and 85% *n*-butyl 4-acetylcinnamate.

In agreement with data reported for Heck reactions of enol ethers,[17] **1a** shows the usual regioselectivity for vinyl ethers. Electron-rich aryl substrates like 4-bromoanisole favor α-arylation, whereas electron-poor aryl derivatives, such as 4-bromoacetophenone, strongly favor β-arylation. Attempts to improve selectivity with different bases and additional salts[18] were not successful. However, a rate enhancement was achieved by using an additional 0.2 equivalent of ammonium salts.

An intriguing characteristic of the new catalysts is their pronounced thermal stability in solution. Heavy precipitation of inactive Pd-black—induced by high reaction temperatures (normally 100–140 °C)—is generally not observed with palladacycles; only trace amounts are found after long reaction periods (>25 h). The thermal stability of palladacycles is certainly a consequence of the cyclometallated structure.[20] P–C bond cleavage and aryl scrambling, both common processes in Pd^{II}–phosphine complexes,[21, 22] are not of any importance at reaction temperatures around 130 °C. The use of palladacycles is therefore particularly advantageous for less reactive substrates.

It was thus assumed that palladacycles could also act as catalysts for the activation of aryl chlorides.[9] First attempts to use **1a** for the reaction of 4-chloroacetophenone with *n*-butyl acrylate under standard reaction conditions failed. In fact, early Pd precipitation occurred if aryl chlorides were treated on their own with the catalyst **1a** above 120 °C. However, certain halide salts (preferably alkali bromides and tetrabutylammonium bromide) induced a considerable activation of the aryl chlorides. As a result, Heck coupling with 4-chlorobenzaldehyde gives a 80% yield of *n*-butyl 4-formylcinnamate in the presence of 0.1 mol% **1a** (TON = 800)!

The results for the C–C coupling reaction of chloroarenes substituted with electron-withdrawing groups are summarized in Table 3. *n*-Butyl acrylate and styrene react similarly, and yields of 50% and 69% were obtained for 4-cyanostilbene and 4-acetylstilbene in the presence of only 0.1 mol% catalyst (TON = 500 and 690 respectively). Even higher TONs were obtainable if lower concentrations of catalyst were used. Thus,

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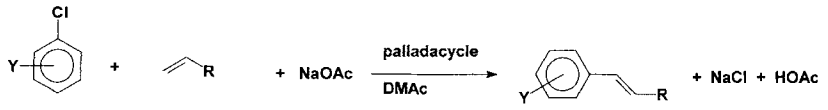
Table 3. Heck olefination of aryl chlorides with palladacycle **1a** as catalyst (Y = 4-CHO, 4-CN, 4-$COCH_3$; R = COOBu, Ph).



No.	R	Aryl halide	Catalyst (mol% Pd)	Additive/promotor (mol%)	Reaction time (h)	Yield (%)	TON (mol product/mol Pd)
1	COOBu	4-chlorobenzaldehyde	**1a** (2)	–	24	12 [a]	6
2	COOBu	4-chlorobenzaldehyde	**1a** (0.2)	LiBr (20)	22	63 [a]	315
3	COOBu	4-chlorobenzaldehyde	**1a** (0.2)	$[NBu_4]Br$ (20)	24	81 [a]	405
4	COOBu	4-chlorobenzaldehyde	**1a** (0.02)	$[NBu_4]Br$ (20)	24	45 [a]	2250
5	COOBu	4-chlorobenzaldehyde	**2b** (0.2)	LiBr (100)	24	40 [a]	200
6	COOBu	4-chlorobenzaldehyde	**2b** (0.2)	LiBr (100)	4	40 [a]	200
7	COOBu	4-chloroacetophenone	**1a** (0.001)	$[NBu_4]Br$ (20)	72	40 [a]	40000
8	COOBu	4-chloroacetophenone	**Pd(OAc)$_2$** (0.001)	PPh_3 (0.002) $[NBu_4]Br$ (20)	72	19 [a]	19000
9	Ph	4-chlorobenzonitrile	**1a** (0.1)	$[NBu_4]Br$ (20)	68	48 [b]	480
10	Ph	4-chloroacetophenone	**1a** (0.1)	$[NBu_4]Br$ (20)	54	69 [b]	690
11	Ph	4-chloroacetophenone	**1a** (0.001)	$[NBu_4]Br$ (20)	69	32 [b]	32000

[a] GLC yield. [b] Isolated by crystallization.

in the presence of 10^{-3} mol% of **1a** TONs of 32000 and 40000 (!) were observed for the reactions of 4-chloroacetophenone with *n*-butyl acrylate and styrene. Although the conversion was not 100% with this low amount of catalyst, the path towards an economic large-scale activation of aryl chlorides for C–C coupling now seems to be open. Previously, the best reported results (TONs of up to 95, catalyst: $[Pd(OAc)_2]$/2 1,4-bis(diisopropylphosphino)butane) for the conversion of aryl chlorides used highly basic and sterically hindered phosphines.[4]

The origin of the dramatic salt effect for the aryl chloride activation is not understood in detail. Although it is known that precipitating palladium is stabilized as a colloid in the presence of tetraalkylammonium halides,[23] and shows a certain activity in Heck reactions, it is unlikely that palladium colloids are responsible for the observed catalyst activity.[24] We now assume that a higher halide concentration yields *anionic* halide-coordinated palladium–phosphine complexes, which are more active than the neutral palladium catalyst systems.[25] Hence, the search for more appropriate anionic promoters looks promising for future improvements of new catalyst systems.

In order to compare the palladacycle **1a** with conventional catalysts, a number of the aforementioned reactions were performed under identical reaction conditions in the presence of $[Pd(OAc)_2]$/2 PPh_3 and of $[Pd(OAc)_2]$/2 P(*o*-Tol)$_3$. We were surprised to find that the catalytic activities for the reaction of activated aryl bromides (e.g., 4-bromobenzaldehyde, 4-bromoacetophenone) with styrene and *n*-butyl acrylate were similar to those of the palladacycles. Even with 10^{-4} mol% of simple $[Pd(OAc)_2]$—without any ligand!—4-acetylstilbene was obtained in 56% yield. This corresponds to a TON of 560000. On the other hand, the palladacycle **1a** displays advantages for Heck reactions of deactivated bromoarenes and chloroarenes. Here, the palladacycle is stable under reaction conditions at 140 °C for several days, whereas equimolar mixtures of $[Pd(OAc)_2]$ and PPh_3 or P(*o*-Tol)$_3$ (P/Pd = 1/1) suffer from early precipitation of palladium black at the same temperature.[26] To exemplify this, the reaction of 4-bromoanisole with *n*-butyl acrylate in the presence of **1a** or an "in situ catalyst" is shown in Figure 2. The isolated complex **1a** exhibited much higher activity and yield of Heck product than a "conventional catalyst" made from equimolar amounts of $[Pd(OAc)_2]$ and P(*o*-Tol)$_3$ (same Pd/P ratio).

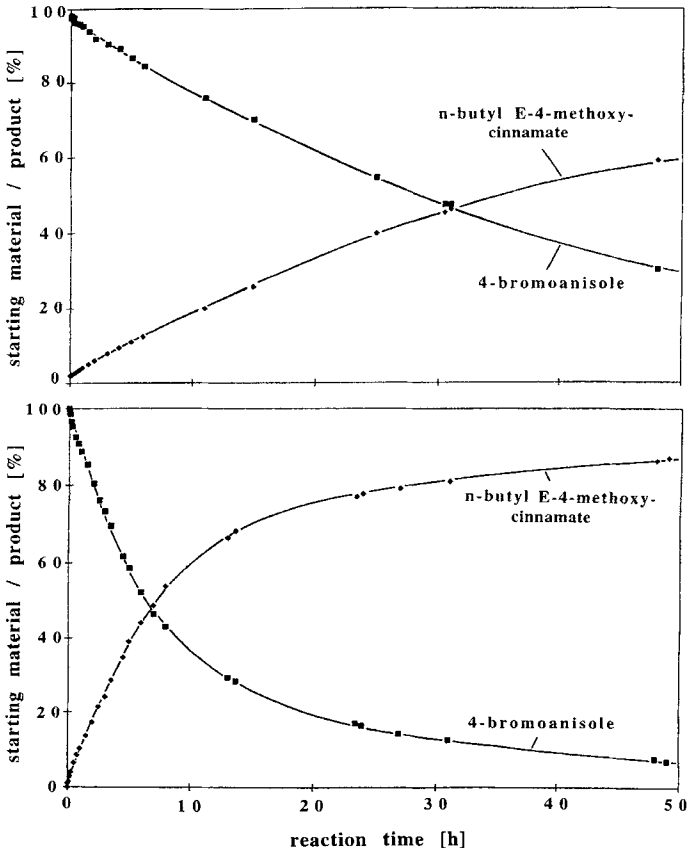


Figure 2. Concentration versus time diagram (GLC) for the Heck-olefination of 4-bromoanisole (as an example of a deactivated bromoarene) with *n*-butyl acrylate at $T = 140$ °C. For reaction conditions, see Table 1. The decrease in 4-bromoanisole ■ (reactant) and increase in *n*-butyl (*E*)-4-methoxycinnamate ● (Heck product) is shown. Top: "in situ catalyst" $[Pd(OAc)_2]$/P(*o*-Tol)$_3$ with Pd:P = 1:1 (1 mol% Pd); bottom: palladacycle **1a** as catalyst (1 mol% Pd).

Deactivated chloroarenes, e.g. chloroanisole, are not applicable as yet, because higher reaction temperatures are necessary for their oxidative addition. More drastic conditions, however, lead to early catalyst decomposition and low yields (< 10% with 0.1 mol% **1a**).

Conclusion

Palladacycles constitute a new class of well-defined catalysts or efficient catalyst precursors for the Heck olefination of haloarenes. An improved catalyst efficiency compared to all previously described palladium-containing catalysts has been realized for the reactions with deactivated aryl bromides and activated aryl chlorides. Here, advantages with regard to conventional catalyst mixtures are based on *high activity at low P/Pd-ratio* and *improved thermal stability* and *lifetime* in solution. In this respect, the reactivity profiles of palladacycles explain why several phosphine equivalents can be saved for Heck reactions. Furthermore, the new catalysts are far less sensitive to air than the conventional Pd^0-based systems.

The rate-enhancing effect of *o*-tolyl groups in the phosphine had already been observed by Heck in the seventies.[27] At that time this finding was explained by the steric effect of *ortho*-substitution;[28] palladacycles were explicitly excluded as active species.[29] This concept must now be revised; indeed, the mixture $[Pd(OAc)_2]/n\,P(o\text{-Tol})_3$ ("Heck catalyst") basically consists of the palladacycle **1a** (evidence from ^{31}P and ^1H NMR). The metallated P–C-chelate ligands presented in this paper are likely to serve as a future concept for catalysis and are attractive alternatives to electron-rich phosphine ligands.[3] As for the mechanism of the palladacycle-catalyzed Heck reaction, more research is necessary to prove either a Pd^0/Pd^{II} or Pd^{II}/Pd^{IV} pathway.[30]

Moreover, we have shown for the first time that Heck reactions of aryl bromides with electron-withdrawing groups can be performed in the presence of simple $[Pd(OAc)_2]/2\,PPh_3$ catalysts with TONs of one to three orders of magnitude higher than those reported to date.

Experimental Section

Palladium(II) acetate and the organophosphines $P(Mes)_3$, $PCy(o\text{-Tol})_2$ and $PCy_2(o\text{-Tol})$ were gifts from Hoechst AG. Other phosphines were either prepared by literature methods[8b, 20a] or obtained from Aldrich or Strem. Other chemicals were from Fluka and Aldrich. NMR spectra (^1H, ^{31}P, ^{13}C) were recorded on a Jeol JMX-GX 400 instrument. NMR multiplicities are abbreviated as follows: s = singlet, d = doublet, dd = double doublet, t = triplet, dt = double triplet, q = quartet, qui = quintet, m = multiplet, br = broad signal. Coupling constants *J* are given in Hz. CI-MS spectra were recorded on a Varian MAT 311 a (150 eV, isobutene). GC-MS spectra were measured on a Hewlett Packard gas chromatograph GC 5890 A equipped with a mass selective detector MS 5970 B. Elemental analyses were carried out by the Microanalytical Laboratory at the TU München. The C–C coupling products and palladium complexes were fully characterized (GC-MS, EA, NMR (^1H, ^{13}C, ^{31}P), CI-MS) and yields were generally determined by gas chromatography. Quantitative analyses were performed on a Hewlett Packard 5980 A instrument using a 12.5 m HP-1 capillary column in conjunction with a flame ionization detector (GC/FID).

Except for the work-up of reaction mixtures, all operations were carried out under argon. *N,N*-dimethylacetamide was distilled prior to use. Other solvents (toluene, diethyl ether, hexane, pentane, CH_2Cl_2) were carefully dried according to standard procedures. Stock solutions of catalyst were used on account of the low concentrations. These were freshly prepared for each reaction and used only once.

General procedure for Heck olefinations: Catalyst solution: the appropriate palladacycle (**1a,b**; **2a,b**, see Table 1; 5×10^{-4}–0.5 mmole) was dissolved in 20 mL of *N,N*-dimethylacetamide. The solution was degassed and purged with argon prior to use.

Reaction mixture: In a 100 mL three-necked flask equipped with a septum inlet, a thermometer and a reflux condenser (Hg bubbler) were placed aryl halide (50 mmole), anhydrous sodium acetate (4.51 g, 55 mmole), diethylene glycol di-*n*-butylether (1 g, GC standard), and *N,N*-dimethylacetamide (30 mL). The reaction mixture was degassed under vacuum, then argon was passed over the condenser for 5 min to ensure an inert reaction atmosphere. *n*-Butyl acrylate (10 mL, 70 mmole) was added last because of the possible loss by evaporation. The reaction mixture was vigorously stirred and heated to the appropriate reaction temperature, at which it was held steady for 10 min; then preheated catalyst solution (60–80 °C) was injected by syringe (start, $t = 0$). For kinetic studies samples of 0.5 mL were withdrawn from the reaction mixture, washed with 5% hydrochloric acid (5 mL) and extracted with CH_2Cl_2 (3.5 mL). The organic phases were removed and sealed in GC vials as required for the gas-chromatographic determination of the yield. Work-up was achieved by pouring the reaction mixture at RT into an excess of water, extracting with CH_2Cl_2 or Et_2O, and drying with $MgSO_4$. After removal of the extraction solvent and *N,N*-dimethylacetamide, the products were purified by distillation or recrystallization.

For the gas-chromatographic determination of the reaction profiles (concentration versus time diagrams) reactant amounts were doubled in order to ensure an approximately constant reaction volume.

Preparation of cyclometallated palladium(II)–phosphine complexes

***trans*-di(μ-acetato)-bis[*o*-(di-*o*-tolylphosphino)benzyl]dipalladium(II) (1a)**: Palladium acetate (4.5 g, 20.0 mmole) was dissolved in toluene (500 mL). To the reddish brown solution was added $P(o\text{-tolyl})_3$ (8.0 g, 26.3 mmol). The bright orange mixture was heated at 50 °C for 3 min and then rapidly cooled to RT. The solvent volume (375 mL) was reduced to a quarter in vacuo, followed by addition of hexane (500 mL) to precipitate the complex. After filtration and drying in vacuo 8.8 g of **1a** was obtained as a yellow solid. Yield: 8.8 mg, 93% referred to $[Pd(OAc)_2]$. A solution of the complex in toluene or CH_2Cl_2 can be further purified by filtration through a bed of Celite®. Recrystallization from toluene/hexane or CH_2Cl_2/hexane gave **1a** as microcrystalline, analytically pure yellow crystals (TG-MS onset temperature: 251 °C). ^1H NMR (400 MHz, −70 °C, CD_2Cl_2): $\delta = 7.31$ (m, 4H, H_{tolyl}), 7.21 (m, 2H, H_{tolyl}), 7.12 (m, 6H, H_{tolyl}), 7.06 (t, 2H, H_{benzyl}, $^3J(H,H) = 7.3$ Hz), 6.92 (m, 4H, H_{tolyl}), 6.70 (t, 2H, H_{benzyl}, $^3J(H,H) = 7.3$ Hz), 6.56 (t, 2H, H_{benzyl}, $^3J(H,H) = 9$ Hz), 6.35 (dd, 2H, H_{benzyl}, $^3J(H,H) = 7.9$ Hz, $^4J(P,H) = 12.2$ Hz), 3.00 (s, 6H, CH_3), 2.81 (dd, 2H, CH_aH_b, $^2J(H_a,H_b) = 14.0$ Hz, $^3J(P,H) = 4.5$ Hz), 2.40 (dd, 2H, CH_aH_b, $^2J(H_a,H_b) = 14.0$ Hz, $^3J(P,H) = 1.8$ Hz), 2.10 (s, 6H, CH_3), 1.91 (s, 6H, CH_3); $^{13}C\{^1H\}$ NMR (100.5 MHz, −70 °C, CD_2Cl_2): $\delta = 178.5$ (s, CH_3CO_2), 157.1 (d, C_{Ar}, $J(P,C) = 31.3$ Hz), 141.1 (d, C_{Ar}, $J(P,C) = 16.0$ Hz), 141.0 (d, C_{Ar}, $J(P,C) = 21.0$ Hz), 133.0 (s, C_{Ar}), 132.5 (d, C_{Ar}, $J(P,C) = 4.6$ Hz), 132.4 (d, C_{Ar}, $J(P,C) = 6.1$ Hz), 131.7 (d, C_{Ar}, $J(P,C) = 8.8$ Hz), 131.4 (d, C_{Ar}, $J(P,C) = 13.7$), 131.3 (d, C_{Ar}, $J(P,C) = 9.9$ Hz), 130.4 (d, C_{Ar}, $J(P,C) = 16.0$ Hz), 129.9 (s, C_{Ar}), 129.1 (d, C_{Ar}, $J(P,C) = 46.2$ Hz), 128.7 (s, C_{Ar}), 128.1 (d, C_{Ar}, $J(P,C) = 33.2$ Hz), 127.6 (d, C_{Ar}, $J(P,C) = 23.7$ Hz), 125.6 (d, C_{Ar}, $J(P,C) = 7.3$ Hz), 125.2 (d, C_{Ar}, $J(P,C) = 7.3$ Hz), 124.9 (d, C_{Ar}, $J(P,C) = 11.4$ Hz), 30.8 (s, CH_2), 24.7 (d, CH_3CO_2, $^4J(P,C) = 3.1$ Hz), 23.0 (d, CH_3, $^3J(P,C) = 13.7$ Hz), 22.2 (d, CH_3, $^3J(P,C) = 6.9$ Hz); $^{31}P\{^1H\}$ NMR (161.9 MHz, −70 °C, CD_2Cl_2): $\delta = 34.2$ (s); IR (KBr): $\tilde{\nu} = 3052$ (m), 3007 (m), 2954 (w), 2925 (m) *n*(CH), 1578 (vs) [*n*(m_2-C=O)], 1468 (s), 1416 (vs) [*n*(m_2-C–O)], 1341 (w), 1282 (w), 1203 (w), 1132 (m), 1069 (m), 1029 (w), 805 (w), 757 (vs), 714 (m), 670 (m), 584 (m), 560 (m), 526 (s), 470 (s) cm^{-1}; MS (150 eV, CI): *m/z* (%) = 939 [$M^+ + H$], 880 [$M^+ - OAc$], 819 [$M^+ - 2\,OAc$], 714 [$\{Pd\{o\text{-}CH_2C_6H_4P(o\text{-}Tol)_2\}_2\}^+$]; $C_{46}H_{46}P_2O_4Pd_2$ (937.62): calcd C 58.93, H 4.94, P 6.61, O 6.83, Pd 22.70; found C 58.89, H 5.06, P 6.92, O 6.47, Pd 21.84.

***trans*-Di(μ-bromo)-bis[*o*-(di-*o*-tolylphosphino)benzyl]dipalladium(II) (1b)**: Tetrabutylammonium bromide (1.61 g, 5.00 mmole) was added to $[Pd_2(OAc)_2\{o\text{-}CH_2C_6H_4P(o\text{-}Tol)_2\}_2]$ (**1a**) (240 mg, 0.26 mmole) dissolved in dichloromethane (20 mL). The mixture was stirred at RT for 1 h. After removal of the solvent, the organic residue was washed with methanol (30 mL) to dissolve the excess tetrabutylammonium salts. The remaining yellow precipitate was filtered and washed again with methanol (2 × 20 mL) and dry pentane (2 × 20 mL). After drying in vacuo **1b** was obtained as a fine yellow powder. Yield: 245 mg, 98% with respect to **1a**. Complex **1b** is not readily soluble in CH_2Cl_2 and *N,N*-dimethylformamide (TG-MS onset temperature: 325 °C). ^1H NMR ([D_7]DMF with the addition of excess NaBr, −70 °C, 400 MHz): $[Pd\{o\text{-}CH_2C_6H_4P(o\text{-Tol})_2\}Br_2]^-$: $\delta = 7.5$–7.0 (m, 10H,

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$H_{tolyl} + H_{benzyl}$), 6.76 (t, 1H, H_{benzyl}, $^3J(H,H) = 8.5$ Hz), 6.59 (t, 1H, H_{benzyl}, $^3J(H,H) = 8.5$ Hz), 4.07 (s, 6H, CH_3), 3.74 (dd, 1H, CH_aH_b, $^2J(H_a,H_b) = 14.0$ Hz, $^3J(PH_a)$ ca. 1.2 Hz), 3.13 (d, 1H, CH_aH_b, $^2J(H_a,H_b) = 14.0$ Hz); $^{31}P\{^1H\}$ NMR (CD_2Cl_2 with the addition of $[NBu_4]Br$, 20 °C, 161.85 MHz): $\delta = 42.3$ (s, $[Pd\{o\text{-}CH_2C_6H_4P(o\text{-}Tol)_2\}Br_2]^-$); MS (150 eV, CI): *m/z* (%) = 981 $[M^+ + H]$, 791 $[\{Pd\{o\text{-}CH_2C_6H_4P(o\text{-}Tol)_2\}_2Br\}^+]$, 569 $[\{Pd\{o\text{-}CH_2C_6H_4P(o\text{-}Tol)_2\}Br_2\}^+]$, 490 $[\{Pd\{o\text{-}CH_2C_6H_4P(o\text{-}Tol)_2\}Br\}^+]$; $C_{42}H_{40}Br_2P_2Pd_2$ (979.33): calcd C 51.51, H 4.12, P 6.33, Br 16.32, Pd 21.73; found C 51.63, H 4.34, P 6.41, Br 16.02, Pd 20.96.

***trans*-Di(μ-chloro)-bis[*o*-(di-*o*-tolylphosphino)benzyl]dipalladium(II) (1c)**: Tetrabutylammonium chloride (1.00 g, 3.38 mmole) was added to $[Pd_2(OAc)_2\{o\text{-}CH_2C_6H_4P(o\text{-}Tol)_2\}_2]$ (**1a**) (250 mg, 0.27 mmole) dissolved in CH_2Cl_2 (20 mL). The mixture was stirred at RT for 1 h. After removal of the solvent, the organic residue was washed with methanol (30 mL) to dissolve the excess tetrabutylammonium salts. The remaining yellow precipitate was filtered and washed again with methanol (2 × 20 mL) and dry pentane (2 × 20 mL). After drying in vacuo **1c** was obtained as a fine yellow powder. Yield: 237 mg, 100% referred to **1a**). Complex **1c** was not readily soluble in CH_2Cl_2 and *N*,*N*-dimethylformamide (TG-MS onset temperature: 331 °C). $^{31}P\{^1H\}$ NMR (CD_2Cl_2 with the addition of $[NBu_4]Cl$, 20 °C, 161.85 MHz): $\delta = 39.3$ (s, $[Pd\{o\text{-}CH_2C_6H_4P(o\text{-}Tol)_2\}Cl_2]^-$); MS (150 eV, CI): *m/z* (%) = 891 $[M^+ + H]$, 481 $[\{Pd\{o\text{-}CH_2C_6H_4P(o\text{-}Tol)_2\}Cl_2\}^+]$, 444 $[\{Pd\{o\text{-}CH_2C_6H_4P(o\text{-}Tol)_2\}Cl\}^+]$; $C_{42}H_{40}Cl_2P_2Pd_2$ (890.43): calcd C 56.65, H 4.53, P 6.96, Cl 7.96, Pd 23.90; found C 56.29, H 4.57, P 7.04, Cl 8.14, Pd 23.49.

***trans*-Di(μ-acetato)-bis[*o*-(dimesitylphosphino)-3,5-dimethylbenzyl]dipalladium(II) (2a)**: Palladium acetate (1.30 g, 5.80 mmole) was dissolved in toluene (200 mL). To the reddish-brown solution was added trimesitylphosphine (2.30 g, 5.91 mmole). The mixture, which gradually turned dark yellow, was stirred at RT for approximately 12 h. After filtration through a bed of Celite, the mixture was reduced to dryness in vacuo. The organic residue was triturated with cold Et_2O (10–20 mL) and stirred at 0 °C until a voluminous yellow precipitate was obtained. The latter was filtered and washed with a small portion of **cold** ether and pentane (2 × 5 mL). After drying in vacuo **2a** was obtained as a yellow solid. Yield: 2.60 g, 81% with respect to $[Pd(OAc)_2]$. For analytically pure **2a** the product had to be chromatographed to remove traces of free $P(Mes)_3$ (silica/50% CH_2Cl_2/*n*-hexane). Recrystallization of the complex leads to major losses because **2a** has the same solubility characteristics as trimesitylphosphine (solubility in Et_2O and *n*-hexane).[31] $P\{^1H\}$ NMR (CD_2Cl_2, −70 °C, 161.85 MHz): $\delta = 25.6$ (s); MS (150 eV, CI): *m/z* (%) = 1106 $[M^+]$, 1047 $[M^+ - OAc]$, 988 $[M^+ - 2\,OAc]$, 881 $[\{Pd\{o\text{-}CH_2C_6H_2(CH_3)_2P(Mes)_2\}_2\}^+]$; $C_{58}H_{70}P_2O_4Pd_2$ (1105.94): calcd C 62.99, H 6.38, P 5.60, O 5.79, Pd 19.24; found C 63.32, H 6.06, P 5.94, O 5.54, Pd 19.52.

***trans*-Di(μ-bromo)-bis[*o*-(dimesitylphosphino)-3,5-dimethylbenzyl]dipalladium(II) (2b)**:

Method A: Tetrabutylammonium bromide (5.0 g, 15.5 mmole) was added to $[Pd_2(OAc)_2\{o\text{-}CH_2C_6H_2(CH_3)_2P(Mes)_2\}_2]$ (**2a**, 1.23 g, 1.11 mmole) dissolved in CH_2Cl_2 (30 mL). The mixture was stirred at RT for 1 h. After removal of the solvent in vacuo, the organic residue was washed with methanol (30 mL) to dissolve surplus tetrabutylammonium salts. The remaining yellow precipitate was filtered, washed again with methanol (2 × 20 mL) and dry pentane (2 × 20 mL) and dried in vacuo to afford **2b** as a fine yellow powder. Yield: 1.1 g, 86% with respect to **2a**). Recrystallization from CH_2Cl_2/*n*-hexane gave microcrystalline needles of complex **2b**.

Method B: Trimesitylphosphine (8.15 g, 21.0 mmole) was added to palladium acetate (4.5 g, 20.0 mmole) dissolved in toluene (approximately 500 mL). The mixture was stirred at RT for 12 h, filtered through a bed of Celite and reduced in vacuo to dryness. The residue was redissolved in 1–1.5 L of CH_2Cl_2, and tetrabutylammonium bromide (45 g, 140 mmole) was added to the solution. After additional stirring for 6 h the solvent was removed in vacuo and the yellow residue was triturated with 300 mL of methanol. The yellow precipitate was filtered and washed with methanol (3 × 200 mL) and dry pentane (2 × 200 mL). After drying in vacuo **2b** was obtained as a yellow powder. Yield: 9.3 g, 81% with respect to $[Pd(OAc)_2]$. ^1H NMR (CD_2Cl_2, 20 °C, 400 MHz): $\delta = 6.84$ (d, 8H, $m\text{-}H_{Mes}$, $^4J(P,H)$ ca. 3 Hz), 6.75 (s, 2H, $m\text{-}H_{benzyl}$), 6.53 (s, 2H, $m\text{-}H_{benzyl}$), 3.28 (s, 4H, CH_2), 2.34 (s, 24H, *o*-CH_3Mes), 2.28 (s, 12H, *p*-CH_3 Mes), 2.24 (s, 6H, *p*-CH_3 benzyl), 1.64 (s, 6H, *o*-CH_3 benzyl); $^{31}P\{^1H\}$ NMR (CD_2Cl_2, 20 °C, 161.85 MHz): $\delta = 30.2$ (s); MS (150 eV, CI): *m/z* (%) = 1149 $[M^+ + H]$, 1070 $[M^+ + H - Br]$, 881 $[\{Pd\{o\text{-}CH_2C_6H_2(CH_3)_2P(Mes)_2\}_2\}^+]$, 493 $[\{Pd\{o\text{-}CH_2C_6H_2(CH_3)_2P(Mes)_2\}\}^+]$, 388 $[\{P(Mes)_3\}^+]$; $C_{54}H_{64}Br_2P_2Pd_2$ (1147.66): calcd C 56.52, H 5.62, P 5.39, Br 13.93, Pd 18.54; found C 56.63, H 5.92, P 5.41, Br 13.85, Pd 19.12.

***trans*-Di(μ-chloro)-bis[*o*-(dimesitylphosphino)-3,5-dimethylbenzyl]dipalladium(II) (2c)**: This was prepared in a manner analogous to tetrabutylammonium chloride, Methods A or B. $^{31}P\{^1H\}$ NMR (CD_2Cl_2, 20 °C, 161.85 MHz): $\delta = 28.5$ (s); MS (150 eV, CI): *m/z* (%) = 1060 $[M^+ + H]$, 1025 $[M^+ + H - Cl]$, 881 $[\{Pd\{o\text{-}CH_2C_6H_2(CH_3)_2P(Mes)_2\}_2\}^+]$, 493 $[\{Pd\{o\text{-}CH_2C_6H_2(CH_3)_2P(Mes)_2\}\}^+]$, 388 $[\{P(Mes)_3\}^+]$; $C_{54}H_{64}Cl_2P_2Pd_2$ (1058.75): calcd C 61.26, H 6.09, P 5.85, Cl 6.70, Pd 20.10; found C 61.56, H 5.98, P 5.47, Cl 6.85, Pd 19.92.

Di(μ-acetato)-bis[*o*-(*t*-butyl-*o*-tolylphosphino)benzyl]dipalladium(II) (3a): *t*-Butyl-di(*o*-tolyl)phosphine (5.68 g, 21.0 mmole) was added to a solution of palladium acetate (4.5 g, 20.0 mmole) in toluene (400 mL). The mixture was stirred at 60 °C for 5 min. After removal of the solvent in vacuo, the organic residue was washed with Et_2O (50 mL). The remaining precipitate was isolated, dried, and redissolved in CH_2Cl_2. The resulting solution was filtered through a bed of Celite to remove traces of palladium black and then evaporated to dryness. Recrystallization from CH_2Cl_2/*n*-hexane at −30 °C gave **3a** as almost colorless crystals containing 0.3–0.5 equiv of hexane in the crystal lattice. Yield: 8.2 g, 94% with respect to $[Pd(OAc)_2]$. ^1H NMR (CD_2Cl_2, 20 °C, 400 MHz): $\delta = 7.79$ (m, 2H, H_{benzyl}), 7.36 (t, 2H, H_{Ar}, $^3J(H,H)$ ca. 7.5 Hz), 7.3–7.0 (m, 12H, H_{Ar}), 3.3 (br, 4H, CH_2), 2.3 (br, 6H, CH_3), 1.8 (br, 6H, CH_3), 1.45 (d, 18H, $C(CH_3)_3$, $^3J(P,H) = 14.6$ Hz), 0.8–1.0 (m, hexane); $^{31}P\{^1H\}$ NMR (CD_2Cl_2, 20 °C, 161.85 MHz): $\delta = 65$–63 (br m); (CD_2Cl_2, −90 °C, 161.85 MHz, with integral *I*): $\delta = 63.3$ (s, *trans* isomer, $I = 80\%$), 63.8 (s, *cis* isomer, $I = 20\%$); MS (150 eV, CI): *m/z* (%) = 870 $[M^+ + H]$, 810 $[M^+ - OAc]$, 751 $[M^+ - 2\,OAc]$, 375 $[\{Pd(o\text{-}CH_2C_6H_4P(t\text{-}Bu)(o\text{-}Tol))\}^+]$; $C_{40}H_{50}P_2O_4Pd_2 \cdot 0.3\,C_6H_{14}$ (895.43): calcd C 56.07, H 6.10, P 6.92, O 7.15, Pd 23.77; found C 55.95, H 6.38, P 6.58, O 6.49, Pd 21.88.

Di(μ-acetato)-bis[*o*-(di-*t*-butylphosphino)benzyl]dipalladium(II) (4a): To a solution of palladium acetate (4.5 g, 20.0 mmole) in toluene (400 mL) was added dropwise di(*t*-butyl)(*o*-tolyl)phosphine (5.0 g, 21.2 mmole). The mixture was stirred at RT for approximately 6 h until a milky suspension was obtained. After removal of the solvent in vacuo, the organic residue was washed with Et_2O (40 mL). The remaining precipitate was filtered, dried, and redissolved in CH_2Cl_2 (50 mL). The resulting solution was filtered through a bed of Celite and evaporated to dryness. Recrystallization from CH_2Cl_2/*n*-hexane at −30 °C gave **4a** as colorless crystals. Yield: 7.25 g, 90% with respect to $[Pd(OAc)_2]$. ^1H NMR (CD_2Cl_2, 20 °C, 400 MHz): $\delta = 7.47$ (t, 2H, H_{Ar}, $^3J(H,H) = 7.3$ Hz), 7.25 (m, 4H, H_{Ar}), 7.11 (m, 2H, H_{Ar}), 3.38 (br, 4H, CH_2), 2.0–1.8 (br, 6H, CH_3COO), 1.42 (d, 36H, $C(CH_3)_3$, $^3J(P,H) = 14.0$ Hz); $^{31}P\{^1H\}$ NMR (CD_2Cl_2, 20 °C, 161.85 MHz): $\delta = 96$–93 (br); (CD_2Cl_2, −90 °C, 161.85 MHz, with integral *I*): $\delta = 95.1$ (s, *cis* isomer, $I = 33\%$), 92.0 (s, *trans* isomer, $I = 67\%$); MS (150 eV, CI): *m/z* (%) = 802 $[M^+ + H]$, 742 $[M^+ - OAc]$; $C_{34}H_{54}P_2O_4Pd_2$ (801.55): calcd C 50.95, H 6.79, P 7.73, O 7.98, Pd 26.55; found C 50.62, H 6.95, P 8.24, O 7.57, Pd 26.65.

Di(μ-acetato)-bis[*o*-(cyclohexyl-*o*-tolylphosphino)benzyl]dipalladium(II) (5a): To a solution of palladium acetate (1.75 g, 7.80 mmole) in toluene (200 mL) was added (cyclohexyl)di(*o*-tolyl)phosphine (2.45 g, 8.27 mmole). The mixture was stirred at RT for approximately 6 h. After removal of the solvent in vacuo, the organic residue was washed with Et_2O (30 mL). The remaining precipitate was isolated, dried, and redissolved in toluene (20 mL). The resulting solution was filtered through a bed of Celite and then evaporated to dryness. Recrystallization from CH_2Cl_2/*n*-hexane or toluene/*n*-hexane at −30 °C gave **5a** as pale yellow crystals. Yield: 1.5 g, 42% with respect to $[Pd(OAc)_2]$. ^1H NMR (CD_2Cl_2, 20 °C, 400 MHz): $\delta = 7.4$–6.8 (m, 16H, H_{Ar}), 2.8–2.2 (br m, 4H, CH_2), 2.41 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 1.88 (s, 6H, CH_3COO), 2.0–0.7 (br, 22H, C_6H_{11}); $^{31}P\{^1H\}$ NMR (CD_2Cl_2, 20 °C, 161.85 MHz): $\delta = 58$–57 (br), (CD_2Cl_2, −90 °C, 161.85 MHz, with integral *I*): $\delta = 62$ (br, *trans* isomer, $I = 70\%$), 54 (br, *cis* isomer, $I = 30\%$); MS (150 eV, CI): *m/z* (%) = 923 $[M^+ + H]$, 697 $[\{Pd(o\text{-}CH_2C_6H_4P(o\text{-}Tol)(Cy))_2\}^+]$; $C_{44}H_{54}O_4P_2Pd_2$ (921.66): calcd C 57.34, H 5.91, P 6.72, O 6.94, Pd 23.09; found: C 57.15, H 5.87, P 6.94, O 6.84, Pd 23.02.

Di(μ-bromo)-bis[*o*-(cyclohexyl-*o*-tolylphosphino)benzyl]dipalladium(II) (5b): The preparation proceeds analogously to **6b** by reaction of **5a** with tetrabutylammonium bromide.

Di(μ-acetato)-bis[*o*-(dicyclohexylphosphino)benzyl]dipalladium(II) (6a): The preparation proceeds analogously to **5a** by reaction of palladium acetate with di(cyclohexyl)(*o*-tolyl)phosphine. Yield: 1.45 g of a beige powder, 41% with respect to $[Pd(OAc)_2]$.

Di(μ-bromo)-bis[*o*-(dicyclohexylphosphino)benzyl]dipalladium(II) (6b): To a solution of palladium acetate (4.5 g, 20.0 mmole) in toluene (400 mL) was added di(cyclohexyl)(*o*-tolyl)phosphine (6.35 g, 22.0 mmole). The mixture was stirred at RT for approximately 12 h. After removal of the solvent in vacuo, the organic residue was triturated with Et_2O (30 mL). The remaining precipitate was filtered, dried, and redissolved in CH_2Cl_2 (40 mL). To this solution was added tetrabutylammonium bromide (16.1 g, 50.0 mmole). The mixture was stirred for a further hour and then evaporated to dryness and washed with MeOH (2 × 20 mL) and pentane (2 × 20 mL). The resulting precipitate was recrystallized from CH_2Cl_2/*n*-hexane at −30 °C. After two weeks **6b** was obtained as orange crystals. Yield: 5 g, 53% yield, referred to $[Pd(OAc)_2]$. These contain one equivalent of hexane in the crystal lattice. ^{1}H NMR (CD_2Cl_2, 20 °C, 400 MHz): δ = 7.32 (q, 4H, H_{Ar}, ^3J(H,H) = 7.3 Hz), 7.26–7.14 (m, 4H, H_{Ar}), 3.58 +3.48 (d +d, 4H, *trans* +*cis* CH_2 (benzyl), ^3J(P,H) = 4.9 +3.7 Hz), 2.4–1.0 (br, 44H, C_6H_{11}), 1.0–0.8 (m, 14H, C_6H_{14}); ^{31}P{^{1}H} NMR (CD_2Cl_2, 20 °C, 161.85 MHz, with integral *I*): δ = 79.3 (s, *trans* isomer, *I* = 73%), 77.6 (s, *cis* isomer, *I* = 27%); MS (150 eV, CI): *m*/*z* (%) = 949 [M^+ + H], 868 [M^+ − HBr], 394 [{Pd(P,Cy_2(*o*-Tol))}$^+$], 288 [P,Cy_2(*o*-Tol)$^+$]; $C_{38}H_{56}Br_2P_2Pd_2 \cdot C_6H_{14}$ (1033.59): calcd C 51.13, H 6.83, P 6.00, Br 15.46, Pd 20.59; found C 51.38, H 6.92, P 6.50, Br 15.28, Pd 20.57.

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