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On the Mechanism of Formation of Homocoupled Products in the Carbon–Carbon Cross-Coupling Reaction Catalyzed by Palladium Complexes Containing Rigid Bidentate Nitrogen Ligands: Evidence for the Exchange of Organic Groups between Palladium and the Transmetalating Reagent[1]

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The results of some carbon–carbon coupling reactions of organic halides with organomagnesium, -zinc, and -tin reagents catalyzed by Pd(Ar-BIAN) complexes, i.e., complexes containing the rigid bidentate nitrogen ligands bis(arylimino)acenaphthene, are described. From a detailed mechanistic study on the formation of homocoupled products, especially in the reaction of benzyl bromide with *p*-tolylmagnesium, *p*-tolylzinc, and organotin reagents, it has been shown that the formation of homocoupled products in catalytic cross-coupling reactions proceeds via a mechanism involving the exchange of organic groups between the organopalladium(II) complex, formed after oxidative addition of the organic halide, and the transmetalating reagent. This leads to the formation of a mixture of two organopalladium(II) complexes and two transmetalating reagents, from which cross-coupled and homocoupled products can be formed. The exchange of organic groups is observed in the reaction of organopalladium(Ar-BIAN) complexes with transmetalating reagents, under conditions such that coupling has not yet occurred (by the appropriate choice of temperature, reaction time, and solvent). Other mechanisms which could in principle lead to the formation of homocoupled products, such as halogen–metal exchange, reductive elimination from a Pd(IV) or a dinuclear Pd(II) complex, reactions via free radical pathways, or disproportionation reactions, are excluded on the basis of our experimental data for the Pd(Ar-BIAN)-catalyzed reaction of benzyl bromide with *p*-tolylmagnesium bromide and *p*-tolylzinc chloride.

Introduction

The formation of new carbon–carbon bonds is a key step in many organic reactions. Nickel- and palladium-catalyzed cross-coupling constitutes one of the most versatile reactions leading to new carbon–carbon bonds, as a variety of organic and organometallic substrates can be used, leading to interesting products, e.g., intermediates in natural product synthesis.[2] The coupling generally consists of a joining of an electropositive carbon fragment, derived from an organic halide, acetate, or triflate, and an electronegative carbon fragment derived from an organometallic reagent, such as organomagnesium,[3] -zinc,[4] -tin,[5] -boron,[6] and -fluorosilicate[7] compounds. A basic, generally accepted mechanism for this type of cross-coupling reaction consists of a sequence of oxidative addition, transmetalation, and reductive elimination (Scheme 1).[8]

In these catalytic reactions mainly palladium and nickel complexes bearing phosphine ligands have been used. More recently, examples of the application of palladium complexes with other types of ligands (containing arsenic[9] or nitrogen[10] as the coordinating atoms) have appeared. Apart from cross-coupling, in some cases formation of homocoupled products has been observed (eq 1).[10d-f,11]

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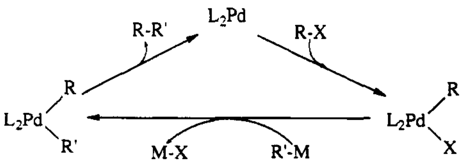
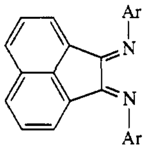
Scheme 1



$$RX + R'M \xrightarrow{[Pd]\ cat.} RR' + RR + R'R' \qquad (1)$$

We were interested in the catalytic activity in cross-coupling reactions of palladium complexes containing bis(arylimino)acenaphthene ligands (Ar-BIAN), i.e., ligands possessing a rigid backbone and nitrogen atoms to coordinate to palladium. This interest stems from the knowledge that the separate steps of the mechanism shown in Scheme 1, especially oxidative addition[12] and reductive elimination,[13] largely depend on the steric and electronic properties of the ligands coordinated to the metal center.


Ar = C_6H_5
p-MeC_6H_4
o-MeC_6H_4
o,o'-$iPr_2C_6H_3$

Ar-BIAN

The choice of Ar-BIAN ligands was based on both electronic and steric grounds. Firstly, because of the good σ-donor and good π-acceptor properties of the diimine system,[14] the Ar-BIAN ligands are capable of stabilizing both higher and lower oxidation states, which might be of importance in an alternating sequence of oxidative addition and reductive elimination. Secondly, the rigidity of the acenaphthene backbone forces the imine N atoms to remain in a fixed *cis* orientation, favoring a chelating coordination to metal complexes. This chelating coordination leads to *cis* complexes of the type Pd(R)(R')(Ar-BIAN), which have both organic groups in a *cis* orientation, thus facilitating reductive coupling from this type of complex (cf. *trans*-M(R)(R')$(PPh_3)_2$ (M = Ni, Pd), which do not eliminate R–R' directly, but generally isomerization is necessary or reductive elimination occurs from a three- or five-coordinate intermediate[15]). The use of Ar-BIAN ligands in catalytic systems is advantageous for mechanistic studies, because the steric properties of the ligand, as well as the steric crowding around the palladium center to which it is coordinated, can be controlled and modified by variation of the aromatic substituent on the imine N atoms and the influence of these substituents on catalytic and stoichiometric reactions can be studied.

The role of chelating ligands in cross-coupling reaction, as compared to monodentate ligands, is not completely clear yet. The use of chelating bidentate phosphine ligands in Grignard cross-coupling reactions has been reported,[3,11h-k] but in cross-coupling reactions with organotin reagents, both decreased[9,16] and improved[17] rates have been reported with chelating diphosphines. One may anticipate that, when the good donor Ar-BIAN ligands are coordinated to the palladium center, the rate of oxidative addition increases,[12] whereas the rate of transmetalation decreases.[9] In a previous communication we have shown that Pd(Ar-BIAN) complexes are active in a variety of cross-coupling reactions, but that in several cases considerable amounts of homocoupled products were formed.[10e] In this paper we report on the Pd(Ar-BIAN)-catalyzed cross coupling of several organic halides with organomagnesium, -zinc, and -tin reagents and a detailed investigation of the mechanism of formation of homocoupled products in some of these reactions. Knowledge about the latter may assist in making a rational choice of catalyst (metal/ligand combination exhibiting maximum efficiency) for a desired carbon–carbon bond forming reaction.

Experimental Section

All reactions were carried out in an atmosphere of dry nitrogen using standard Schlenk techniques. Solvents were carefully dried and distilled prior to use. ^1H NMR spectra were recorded on a Bruker AC 100 (100.13 MHz) and a Bruker AMX 300 spectrometer (300.13 MHz). GC was performed on a Varian 3300 gas chromatograph equipped with a split/splitless injector, a flame ionization detector, and a J&W DB 5 column (length 30 m, 0.53-mm inner diameter, 1.5-μm film thickness). Pd(Ar-BIAN)(dimethyl fumarate) was synthesized by reaction of Pd$(DBA)_2$ with Ar-BIAN[36] and dimethyl fumarate,[18] and $PdCl_2$(Ar-BIAN) was synthesized by reaction of $PdCl_2(PhCN)_2$ with Ar-BIAN;[19] p-TolMgBr[20] and $PhCH_2MgCl$[21] were synthesized according to published procedures. The concentrations of the organomagnesium solutions were determined by titration of 10-mL aliquots with a solution of 2-butanol in xylene (0.500 M) using a phenanthroline indicator.[22] Organic coupling products were characterized by ^1H NMR and GC and were compared with authentic samples.

Pd-Catalyzed Coupling Reactions. $PhCH_2Br$ + *p*-TolMgBr. To a solution of 10.1 mg of $PdCl_2$(Ph-BIAN) (0.020 mmol) in 10 mL of THF was added 0.24 mL of $PhCH_2Br$ (2.02 mmol), followed by 3.0 mL of a 0.733 M p-TolMgBr solution in THF (2.20 mmol). After the mixture was stirred at 20 °C for 1 h, 25 mL of water was added and the mixture transferred to a separatory funnel. The organic products were extracted from the reaction mixture with diethyl ether (3 × 30 mL). The organic layer was back-extracted with water (25 mL) and brine (20 mL), dried on $MgSO_4$, filtered, and evaporated to dryness. Further purification of the organic products was achieved by chromatography over silica using hexane as eluent. The yield was 0.34 g of a white, pasty, product (92%).

The other reactions with organomagnesium reagents and the reactions with p-tolylzinc reagents, prepared in

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situ from $ZnCl_2$ and 1.0 equiv of *p*-tolylmagnesium bromide, were performed in a similar way, under the conditions indicated in Tables 1 and 3.

(*p*-Tol)$_2$. To a solution of 8.9 mg of $PdCl_2$(Ph-BIAN) (0.017 mmol) in 10 mL of THF were added 0.30 g of *p*-bromotoluene (1.75 mmol) and 0.20 g of Mg (8.2 mmol), and the mixture was stirred vigorously at 20 °C. After 17 h, 10 mL of water was added and, after filtration, the mixture was extracted with diethyl ether (2 × 50 mL). The diethyl ether extracts were dried on $MgSO_4$, filtered, and evaporated to dryness. Chromatography of the products over silica using hexane yielded 0.13 g of a white solid (82%).

Homocoupling reactions of bromobenzene and benzyl bromide with magnesium were performed in a similar manner, yielding PhPh (78%) and $PhCH_2CH_2Ph$ (86%), respectively.

Stoichiometric Reactions. PdBr(CH_2Ph)(*p*-Tol-BIAN) + *p*-TolMgBr (−70 °C). To a solution of 18.1 mg of PdBr(CH_2Ph)(*p*-Tol-BIAN) (0.028 mmol) in 5 mL of THF, cooled to −70 °C, was added by syringe 5 drops of a 0.733 M solution of *p*-TolMgBr in THF (excess relative to Pd). The mixture was stirred at −70 °C for 1 min, and then 2 mL of water was added. The mixture was warmed to 20 °C, and dichloromethane was added (20 mL). The water layer was removed and the organic layer evaporated. Characteristic ^{1}H NMR data ($CDCl_3$): 6.44 (d, J = 7.8 Hz), 2.50 (s), 2.38 (s), 2.08 (s) ppm, PdBr(*p*-Tol)(*p*-Tol-BIAN); 3.40 (s), 2.52 (s) ppm, PdBr(CH_2Ph)(*p*-Tol-BIAN); ratio Pd(*p*-Tol):Pd(CH_2Ph) = 2.4:1; 2.90 ppm, $PhCH_2CH_2Ph$; 2.38 ppm, (*p*-Tol)$_2$ (approximately 5% relative to the Pd complexes).

PdBr(CH_2Ph)(*p*-Tol-BIAN) + *p*-TolMgBr (20 °C). To solution of 21.8 mg of PdBr(CH_2Ph)(*p*-Tol-BIAN) (0.034 mmol) in 5 mL of THF at 20 °C was added by syringe 5 drops of a 0.733 M solution of *p*-TolMgBr in THF (excess relative to Pd). The mixture was stirred at 20 °C for 30 min, after which time 5 mL of water was added, followed by 20 mL of dichloromethane. The water layer was removed and the organic layer evaporated to dryness. Characteristic ^{1}H NMR data ($CDCl_3$): 2.90 ppm ($PhCH_2CH_2Ph$); 2.38 ppm ((*p*-Tol)$_2$); 7.88 (d, J = 8.3 Hz), 6.93 (d, J = 7.2 Hz), 2.45 (s) ppm (free *p*-Tol-BIAN); no $PhCH_2$-*p*-Tol observed.

Reactions of PdBr(CH_2Ph)(*p*-Tol-BIAN) with *p*-TolZnCl and of Pd(*p*-Tol)I(*p*-Tol-BIAN) with $PhCH_2MgCl$ were performed under exactly the same conditions. PdBr(CH_2Ph)(*p*-Tol-BIAN) + *p*-TolZnCl (−70 °C): ratio Pd(*p*-Tol):Pd(CH_2Ph) = 2.7:1; about 12% organic coupling products; ratio $PhCH_2$-*p*-Tol (3.94 ppm):$PhCH_2CH_2Ph$ = 95:5. PdBr(CH_2Ph)(*p*-Tol-BIAN) + *p*-TolZnCl (20 °C): ratio $PhCH_2$-*p*-Tol:$PhCH_2CH_2Ph$ = 96:4. Pd(*p*-Tol)I(*p*-Tol-BIAN) + $PhCH_2MgCl$ (−70 °C): no Pd(CH_2Ph) formed; some $PhCH_2$-*p*-Tol (approximately 5% relative to Pd(*p*-Tol)I(*p*-Tol-BIAN)). Pd(*p*-Tol)I(*p*-Tol-BIAN) + $PhCH_2MgCl$ (20 °C): mainly $PhCH_2$-*p*-Tol and uncoordinated *p*-Tol-BIAN formed; no (*p*-Tol)$_2$ observed.

PdBr(CH_2Ph)(*p*-Tol-BIAN) + $SnMe_4$. To a solution of 14.6 mg of PdBr(CH_2Ph)(*p*-Tol-BIAN) (0.023 mmol) in 15 mL of THF was added 6 μL of $SnMe_4$ (0.042 mmol), and the mixture was stirred at 50 °C. After 3 h the mixture was cooled to room temperature and evaporated to dryness. The product was washed with 5 mL of diethyl ether and dried in vacuo. ^{1}H NMR indicated the formation of a mixture of PdBr(CH_2Ph)(*p*-Tol-BIAN) and PdBr(Me)(*p*-Tol-BIAN) (41:59).

The same results were obtained when the reaction was carried out in $CDCl_3$ at 20 °C (15 mg of PdBr(CH_2Ph)(*p*-Tol-BIAN) (0.024 mmol) and 5 μL of $SnMe_4$ (0.036 mmol) in 0.5 mL of $CDCl_3$). The signal at 3.40 ppm (Pd–CH_2Ph) decreased, and a signal at 0.81 ppm (Pd–Me) appeared. Furthermore, the appearance of a signal at 2.34 ppm indicated the formation of $PhCH_2SnMe_3$. However, the reaction was much slower (about 30 h before a mixture of Pd(CH_2Ph) and Pd(Me) in a 1:1 ratio was formed), and as a consequence considerable decomposition occurred.

PdBr(C(O)CH_2Ph)(*p*-Tol-BIAN) + $SnMe_4$. Carbon monoxide was bubbled through a solution of 10 mg of PdBr(CH_2Ph)(*p*-Tol-BIAN) (0.016 mmol) and 5 μL of $SnMe_4$ (0.036 mmol) in 0.5 mL of $CDCl_3$ during 1 min. ^{1}H NMR spectra were taken at several intervals between 15 min and 3 days reaction time. There was no indication for the formation of Pd–Me complexes (0.81 ppm). After 21 h, some decarbonylation had occurred (Pd–C(O)CH_2Ph at 4.14 ppm decreased, and Pd–CH_2Ph at 3.40 ppm appeared) together with the formation of $SnMe_3X$ (0.60 ppm).

Stability of Organopalladium(II) Complexes in Solution. A solution of 25.4 mg of PdBr(CH_2Ph)(*p*-Tol-BIAN) (0.040 mmol) in 5 mL of THF was stirred at 20 °C for 2 h. After that time the solvent was removed under reduced pressure and the product dried in vacuo. The product was analyzed by ^{1}H NMR spectroscopy, which indicated that no reaction occurred and no $PhCH_2CH_2Ph$ (3.00 ppm) was formed. A similar reaction of Pd(*p*-Tol)I(*p*-Tol-BIAN) gave no formation of (*p*-Tol)$_2$ after 2 h in THF at 20 °C either.

Results

Pd(Ar-BIAN)-Catalyzed Coupling of Benzyl and *p*-Tolyl Fragments. The cross coupling between organic halides and organomagnesium or -zinc reagents is efficiently catalyzed by 1% of a $PdCl_2$(Ar-BIAN) or Pd(Ar-BIAN)(dimethyl fumarate) catalyst in THF at 20 °C, whereas reactions with organotin reagents are best performed with 1% of a Pd(Ar-BIAN)(dimethyl fumarate) catalyst in dimethylformamide (DMF) at 50 °C[10e,f] (Table 1). The Pd(Ph-BIAN)-catalyzed coupling of *p*-iodotoluene with benzylmagnesium chloride and that of benzyl bromide with (*p*-tolyl)tributyltin have been reported before[10e,f] but are included here for comparison.

The selectivity of the coupling reaction depends very much on the substrates used. Coupling of *p*-iodotoluene with benzylmagnesium chloride leads almost exclusively to cross-coupled product (98%). The observed bibenzyl arises from the in situ reduction of the $PdCl_2$(Ph-BIAN) catalyst (1%) and from bibenzyl present in the Grignard reagent. On the contrary, the coupling reaction of benzyl bromide with *p*-tolylmagnesium bromide gives mainly the homocoupled products bibenzyl and bi-*p*-tolyl (the deviation from a 1:1 ratio of these products can be ascribed to the presence of some bi-*p*-tolyl in the Grignard reagent), together with a small amount of cross-coupled *p*-benzyltoluene (7–9%). The selectivity for cross coupling can be increased by the use of *p*-tolylzinc chloride instead of *p*-tolylmagnesium bromide (33–38% $PhCH_2$-*p*-Tol), and complete selectivity for cross coupling (>99%) can be achieved by the use of (*p*-tolyl)trialkyltin reagents, (*p*-Tol)SnR_3 (R = Me, Bu). The greater tendency for homocoupling in reactions with organomagnesium compounds as compared to organozinc and -tin reagents has also been observed in other cross-coupling reactions.[10e,f,11c,e,h–k]

Table 1. Palladium-Catalyzed Coupling of Benzyl and *p*-Tolyl Halides with *p*-Tolyl and Benzyl Transmetalating Reagents[a]

reactants	catalyst and conditns[b]	% PhCH$_2$-*p*-Tol	% (PhCH$_2$)$_2$	% (*p*-Tol)$_2$
p-TolI + PhCH$_2$MgCl	PdCl$_2$(Ph-BIAN), 16 h	98	2	0
p-TolI + *p*-TolMgBr	PdCl$_2$(Ph-BIAN), 16 h			100
p-TolBr + PhCH$_2$MgCl	PdCl$_2$(Ph-BIAN), 4 h[c]	1	0	0
p-TolBr + *p*-TolMgBr	PdCl$_2$(Ph-BIAN), 4 h[d]			9
PhCH$_2$Br + *p*-TolMgBr	PdCl$_2$(Ph-BIAN)	9	44	47
PhCH$_2$Br + *p*-TolMgBr	PdCl$_2$(*p*-Tol-BIAN)	7	44	49
PhCH$_2$Br + *p*-TolMgBr	PdCl$_2$(Ph-BIAN) + styrene[e]	7	40	53
PhCH$_2$Br + *p*-TolMgBr	PdCl$_2$(PPh$_3$)$_2$	30	31	39
PhCH$_2$Br + *p*-TolMgBr	PdCl$_2$(dppe)[f]	30	32	38
PhCH$_2$Br + *p*-TolMgBr	PdCl$_2$(bpy)	2	45	53
PhCH$_2$Br + *p*-TolZnCl	PdCl$_2$(Ph-BIAN)	33	31	36
PhCH$_2$Br + *p*-TolZnCl	PdCl$_2$(*p*-Tol-BIAN)	34	30	36
PhCH$_2$Br + *p*-TolZnCl	PdCl$_2$(*o,o'*-*i*-Pr$_2$C$_6$H$_3$-BIAN)	33	28	39
PhCH$_2$Br + *p*-TolZnCl	PdCl$_2$(Ph-BIAN) + *m*-(NO$_2$)$_2$C$_6$H$_4$[g]	38	24	38
PhCH$_2$Br + *p*-TolSnR$_3$[h]	Pd(Ph-BIAN)(dimethyl fumarate)	>99	0	0

[a] Abbreviations used: Me = CH$_3$, *n*-Bu = (CH$_2$)$_3$CH$_3$, Ph = C$_6$H$_5$, *p*-Tol = *p*-MeC$_6$H$_4$, bpy = 2,2'-bipyridine, dppe = Ph$_2$PCH$_2$CH$_2$PPh$_2$. [b] Unless noted otherwise, reactions were carried out in THF at 20 °C for 1 h, employing 1 mol % of the indicated catalyst. Conversion was complete within the indicated time. Isolated yields, after chromatographic workup: PhCH$_2$Br + *p*-TolMgBr/*p*-TolZnCl (90–95%), PhCH$_2$Br + *p*-TolSnR$_3$ (75%), *p*-TolI + PhCH$_2$MgCl (85%). For incomplete reactions the yield was not determined. [c] 99% unreacted *p*-TolBr present. [d] 91% unreacted *p*-TolBr present. [e] One equivalent relative to benzyl bromide. [f] 11% conversion after 1 h. [g] One equivalent relative to palladium. [h] R = Me, *n*-Bu; the reaction was carried out in dimethylformamide at 50 °C.

The Pd(Ar-BIAN)-catalyzed reaction of benzyl bromide with *p*-tolylzinc chloride is not influenced by the addition of styrene (1 equiv relative to benzyl bromide) or *m*-dinitrobenzene (1 equiv relative to Pd), neither in the rate nor in the product distribution. Furthermore, the product distribution is not affected by the steric bulk of the aromatic substituent on the N atoms of the Ar-BIAN ligand coordinated to the palladium center, as appears from the comparable product distribution for the PdCl$_2$(*p*-Tol-BIAN)- and the PdCl$_2$(*o,o'*-*i*-Pr$_2$C$_6$H$_3$-BIAN)-catalyzed reactions. When PdCl$_2$(PPh$_3$)$_2$ or PdCl$_2$(dppe) (dppe = Ph$_2$PCH$_2$CH$_2$PPh$_2$) is employed as a catalyst for the coupling of benzyl bromide with *p*-tolylmagnesium bromide, the reaction is much slower, but the selectivity for cross coupling has increased compared to the selectivity when Pd(Ar-BIAN) catalysts are used. In the case of a PdCl$_2$(bpy) catalyst (bpy = 2,2'-bipyridine) the rate and product formation are comparable to those in the PdCl$_2$(Ar-BIAN)-catalyzed reaction.

Rate of the Coupling Reactions. The Pd(Ar-BIAN)-catalyzed reactions of benzyl bromide with *p*-tolylmagnesium bromide and *p*-tolylzinc chloride are fast and are completed within 1 h at 20 °C with 0.1% of catalyst. The coupling of *p*-tolyl halides with benzylmagnesium chloride at 20 °C is slower: When 1% of catalyst is used, the reaction of *p*-iodotoluene requires 16 h to go to completion, whereas the coupling of *p*-bromotoluene only gave minor conversions with both benzylmagnesium chloride and *p*-tolylmagnesium bromide even after 20 h. Quantitative data of the Pd(Ar-BIAN)-catalyzed coupling between benzyl bromide and *p*-tolylmagnesium bromide were obtained from experiments with a substrate:catalyst ratio of 10^5:1 (Figure 1).

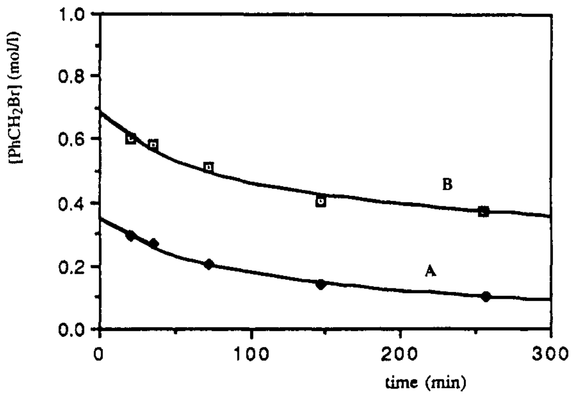


Figure 1. Conversion of benzyl bromide versus the reaction time in the PdCl$_2$(Ph-BIAN)-catalyzed reaction of benzyl bromide with *p*-tolylmagnesium bromide in THF at 20 °C ([PdCl$_2$(Ph-BIAN)] = 3.41 × 10^{-6} M; [*p*-TolMgBr] = 0.350 M; [PhCH$_2$Br] = 0.345 M (A), 0.689 M (B)).

Table 2. Turnover Numbers[a] **for the Palladium-Catalyzed Coupling of Benzyl Bromide with *p*-Tolylmagnesium Bromide**[b]

catalyst, concn (M)	concn, M PhCH$_2$Br	concn, M *p*-TolMgBr	turnover[a]
PdCl$_2$(Ph-BIAN), 3.41 × 10^{-6}	0.345	0.350	505
PdCl$_2$(Ph-BIAN), 3.41 × 10^{-6}	0.689	0.350	886
PdCl$_2$(Ph-BIAN), 3.41 × 10^{-6}	0.345	0.703	490
PdCl$_2$(Ph-BIAN), 3.41 × 10^{-6} [c]	0.345	0.350	458
PdCl$_2$(PPh$_3$)$_2$, 3.43 × 10^{-4}	0.345	0.378	2.1
PdCl$_2$(dppe), 3.51 × 10^{-3}	0.345	0.386	0.2[d]

[a] In (mol of PhCH$_2$Br)·(mol of Pd)$^{-1}$·min^{-1}. [b] Reactions were carried out in THF at 20 °C. The turnover number was calculated after 50% conversion of benzyl bromide. [c] In the presence of styrene (0.358 M). [d] After 11% conversion (1-h reaction time).

Turnover numbers for the first 50% conversion of the Pd(Ph-BIAN)-catalyzed reaction, which were calculated from the half-life times of the reactions, have been summarized in Table 2, together with the data for the Pd(PPh$_3$)$_2$-catalyzed (0.1% catalyst) and the Pd(dppe)-catalyzed (1% catalyst) reactions. From these data it is clear that the Pd(Ar-BIAN)-catalyzed reaction is much faster than the Pd(phosphine)-catalyzed reactions, which is not a simple chelate effect since the Pd(dppe)-catalyzed reaction is slower than the Pd–triphenylphosphine-catalyzed reaction. Furthermore, the rate increases with increasing concentration of benzyl bromide, but is not affected by the concentration of *p*-tolylmagnesium bromide, indicating that the oxidative addition of benzyl bromide to palladium is the rate-determining step.

Reactions in the Absence of a Pd Catalyst. In the absence of a Pd(Ar-BIAN) catalyst, benzyl bromide did not react with *p*-tolylzinc and -tin reagents: under the similar conditions of the catalytic coupling, but omitting the Pd(Ar-BIAN) catalyst, benzyl bromide was recovered quantitatively as the only organic product. However, with *p*-tolylmagnesium bromide, after hydrolytic workup small amounts of bibenzyl, bi-*p*-tolyl, and *p*-bromotoluene were observed in the reaction mixture (about 5% relative to benzyl bromide after 1 h and 15% after 4 h). These results indicate a slow exchange between the organic groups of the organic halide and the Grignard reagent, leading to a mixture of benzyl bromide, *p*-bromotoluene, benzylmagnesium bromide, and *p*-tolylmagnesium bromide (eq 2). This kind of exchange has been observed before between several organic halides and organomagnesium halides (in the absence and in the presence of metal salts),[23] but no exchange has been observed between benzyl bromide and phenylmagnesium bromide in the absence of transition metal salts.[24]

$$PhCH_2Br + (p\text{-Tol})MgBr \rightleftharpoons p\text{-Tol-Br} + (PhCH_2)MgBr \quad (2)$$

Benzyl bromide reacted with benzylmagnesium chloride at 20 °C within 15 min to give bibenzyl, both in the absence and in the presence of a Pd(Ar-BIAN) catalyst. However, benzyl chloride reacted only slowly with benzylmagnesium chloride at 0 °C (20% conversion after 2 h), whereas the palladium-catalyzed coupling was much faster (100% conversion within 2 h). A variety of benzylic halides have been reported to react with organomagnesium halides, in the absence of a transition metal catalyst, to the corresponding bibenzyls as the major product.[25] In the absence of a palladium catalyst, *p*-bromotoluene and *p*-iodotoluene did not react with benzylmagnesium chloride at 20 °C, similar to the reported unreactivity of bromobenzene toward benzylmagnesium chloride in the absence of a catalyst.[24]

Pd(Ar-BIAN)-Catalyzed Homocoupling of Organic Halides. Homocoupled products have been synthesized in THF at 20 °C by the reaction of the organic halide with excess magnesium turnings or zinc dust in the presence of 1% of a $PdCl_2$(Ph-BIAN) catalyst. Bromobenzene, *p*-bromotoluene, and benzyl bromide were converted quantitatively into biphenyl, bi-*p*-tolyl, and bibenzyl, respectively, within 16 h (eqs 3 and 4). In the absence of magnesium or zinc no reaction of benzyl bromide occurred in the presence of 1% of a $PdCl_2$(Ph-BIAN) or $PdBr(CH_2Ph)$(*p*-Tol-BIAN) catalyst, indicating that the presence of a reducing agent is necessary to induce catalytic homocoupling.

$$p\text{-}RC_6H_4Br \xrightarrow{1\%\ [Pd(II)],\ excess\ Mg} (p\text{-}RC_6H_4)_2 \quad (R = H, Me) \quad (3)$$

$$PhCH_2Br \xrightarrow{1\%\ [Pd(II)],\ excess\ Mg} PhCH_2CH_2Ph \quad (4)$$

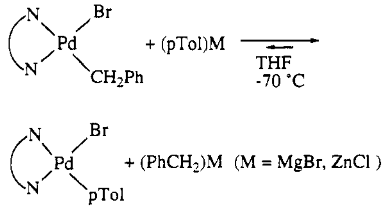
Coupling of Allylic Halides with *p*-Tolylmagnesium Bromide. The reaction of allyl bromide with *p*-tolylmagnesium bromide takes place at 20 °C in THF without the addition of a catalyst and proceeds efficiently (complete conversion within 1 h), leading to *p*-allyltoluene and bi-*p*-tolyl in a ratio of 9:1 (Table 3). The uncatalyzed reaction of allylic halides with arylmagnesium halides has been described previously.[26] Addition of 1% of a $PdCl_2$(Ar-BIAN) catalyst increased both the rate of this reaction and the amount of homocoupled bi-*p*-tolyl. The ratio of cross-coupling to homocoupling is strongly influenced by the aromatic groups on the N atoms of the Ar-BIAN ligand and increased in the order $C_6H_5 \approx p\text{-}MeC_6H_4 < o\text{-}MeC_6H_4 < o,o'\text{-}i\text{-}Pr_2C_6H_3$. Increasing the amount of $PdCl_2$(Ph-BIAN) catalyst to 5% had only a minor effect on the product distribution, whereas the amount of homocoupling increased by 9% when the amount of $PdCl_2$(*o*-Tol-BIAN) catalyst was raised to 5%.

Table 3. Coupling of Allyl Bromide with *p*-Tolylmagnesium Bromide[a]

catalyst	% *p*-allyltoluene	% $(p\text{-Tol})_2$
none	90	10
$PdCl_2$(Ph-BIAN)[b]	62	38
$PdCl_2$(Ph-BIAN) (5%)	58	42
$PdCl_2$(*o*-Tol-BIAN)	76	24
$PdCl_2$(*o*-Tol-BIAN) (5%)	67	33
$PdCl_2(o,o'\text{-}i\text{-}Pr_2C_6H_3\text{-BIAN})$	86	14
$PdCl_2$(bpy)	52	48

[a] Reactions were carried out in THF at 20 °C by using 1 mol % of catalyst, unless indicated otherwise. Complete conversion was achieved in all cases within 1 h. [b] Exactly the same results were obtained when Pd(Ph-BIAN)(dimethyl fumarate) was used as a catalyst.

Stoichiometric Reactions of Organopalladium(II) Complexes with Transmetalating Reagents. Reaction of $PdBr(CH_2Ph)$(*p*-Tol-BIAN) with *p*-tolylmagnesium bromide in THF at 20 °C led to the formation of the homocoupled products bibenzyl and bi-*p*-tolyl in an approximately 1:1 ratio and free *p*-Tol-BIAN, but no cross-coupled *p*-benzyltoluene was detected by ^{1}H NMR (<5%). When *p*-tolylzinc chloride was employed as the transmetalating reagent, mainly cross-coupled *p*-benzyltoluene and only a small amount of bibenzyl were formed. When the reaction of $PdBr(CH_2Ph)$(*p*-Tol-BIAN) with *p*-tolylmagnesium bromide or *p*-tolylzinc chloride was carried out at −70 °C for very short periods (≤1 min), some coupled organic products were observed but in a relatively small amount (5–10% relative to the palladium complexes). From the ^{1}H NMR spectrum of the reaction mixture it appears clearly that, apart from some unreacted Pd–benzyl complex, a new palladium complex was formed (eq 5), which was identified as PdBr(*p*-Tol)(*p*-Tol-BIAN) (it showed ^{1}H resonances comparable to Pd(*p*-Tol)I(*p*-Tol-BIAN), synthesized independently via oxidative addition of *p*-iodotoluene[27]). Reaction of $PdBr(CH_2Ph)$(*p*-Tol-BIAN) with (*p*-tolyl)tributyltin in $CDCl_3$ or THF at 20 °C did not lead to any formation of Pd(*p*-Tol) complexes, and only slow formation of $p\text{-TolCH}_2Ph$ was observed (about 20% after 20 h). Conversely, when Pd(*p*-Tol)I(*p*-Tol-BIAN) was reacted with benzylmagnesium chloride, no reaction occurred at −70 °C during short reaction times, whereas at 20 °C only cross-coupled $PhCH_2$-*p*-Tol and free *p*-Tol-BIAN were observed.



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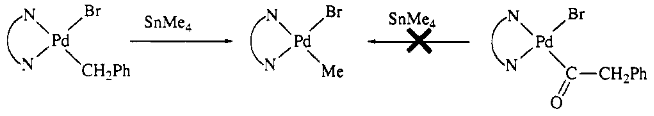
Scheme 2



Reaction of [Pd(η^3-allyl)(*p*-Tol-BIAN)]Br with *p*-tolylmagnesium bromide at −70 °C for 1 min led to the formation of a mixture of PdBr(*p*-Tol)(*p*-Tol-BIAN), *p*-$\mathrm{Tol_2}$, and $[\mathrm{PdBr}(\eta^3\text{-allyl})]_2$, whereas the same reaction at 20 °C yielded mainly $(p\text{-Tol})_2$.

In the reaction of $\mathrm{PdBr(CH_2Ph)}$(*p*-Tol-BIAN) with $\mathrm{SnMe_4}$, under conditions for which cross-coupling is very slow, e.g., in THF at 50 °C or in $\mathrm{CDCl_3}$ at 20 °C,[10e,f] formation of PdBr(Me)(*p*-Tol-BIAN) was observed, indicating that under these conditions exchange of the organic groups between palladium and the transmetalating reagent occurred (Scheme 2). Such an exchange has been described for the similar reaction of $\mathrm{PdBr(CH_2Ph)(PPh_3)_2}$ with $\mathrm{SnMe_4}$, giving initially $\mathrm{PdBr(Me)(PPh_3)_2}$ and $\mathrm{PhCH_2SnMe_3}$, which then reacted to give ethylbenzene.[28]

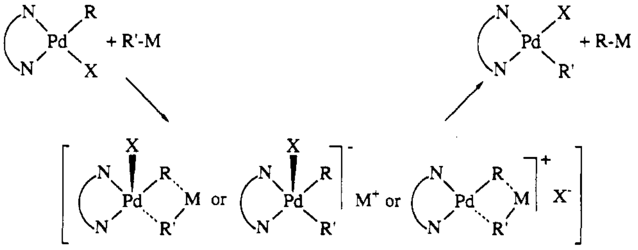
Exchange of organic groups did not occur when carbon monoxide was bubbled through a mixture of $\mathrm{PdBr(CH_2Ph)}$(*p*-Tol-BIAN) and $\mathrm{SnMe_4}$. In this case a $\mathrm{PdBr(C(O)CH_2Ph)}$(*p*-Tol-BIAN) complex was formed instantaneously,[29] which did not react with $\mathrm{SnMe_4}$ in chloroform at 20 °C: no Pd–Me complex was observed (15 min–72 h) in the reaction mixture (Scheme 2). After 20 h, some decarbonylation product, $\mathrm{PdBr(CH_2Ph)}$(*p*-Tol-BIAN), and some $\mathrm{Me_3SnX}$ (X = Br, Cl) were formed, but these reactions were rather slow. After 72 h, most of the acyl complex $\mathrm{PdBr(C(O)CH_2Ph)}$(*p*-Tol-BIAN) had disappeared and the deinsertion product $\mathrm{PdBr(CH_2Ph)}$(*p*-Tol-BIAN) and $\mathrm{Me_3SnX}$ (X = Cl, Br) were present in the reaction mixture in a 1.1:1 ratio.

Discussion

Exchange of Organic Groups in Relation to the Formation of Homocoupled Products. The cross-coupling reaction of benzyl bromide with *p*-tolylmagnesium bromide and *p*-tolylzinc chloride gave the homocoupled bibenzyl and bi-*p*-tolyl as the main products. The formation of homocoupled products in cross-coupling reactions has been observed previously,[10d–f,11] but detailed mechanistic studies of the reactions which could possibly lead to the formation of homocoupled products have not been reported.

In view of our results described above, the obvious explanation for the formation of homocoupled products in the Pd(Ar-BIAN)-catalyzed reactions is the exchange of organic groups between the organopalladium complex formed after oxidative addition and the transmetalating reagent, according to eq 5. Direct evidence obtained for this conclusion is the observation of this exchange of organic groups under conditions for which cross-coupling has not (yet) taken place, for reactions which produce homocoupled products under catalytic conditions. Thus, reaction of $\mathrm{PdBr(CH_2Ph)}$(*p*-Tol-BIAN) with *p*-tolylmagnesium bromide or *p*-tolylzinc chloride at −70 °C for short periods (≤1 min) yielded PdBr(*p*-Tol)(*p*-Tol-BIAN) (eq 5), whereas the same reaction at 20 °C as well as the catalytic reaction between benzyl bromide and *p*-tolylmagnesium bromide or *p*-tolylzinc chloride produced homocoupled products. On the contrary, reaction of $\mathrm{PdBr(CH_2Ph)}$(*p*-Tol-BIAN) with (*p*-tolyl)trialkyltin did not lead to the formation of any PdBr(*p*-Tol)(*p*-Tol-BIAN), whereas the catalytic coupling of benzyl bromide with (*p*-tolyl)trialkyltin gave exclusively cross-coupled product. The reaction of Pd(*p*-Tol)I(*p*-Tol-BIAN) with benzylmagnesium chloride at −70 °C did not lead to benzyl/*p*-tolyl exchange, and the same reaction at 20 °C, as well as the Pd(Ar-BIAN)-catalyzed coupling of *p*-iodotoluene with benzylmagnesium chloride, gave (almost) exclusively cross-coupled *p*-benzyltoluene.

Scheme 3



The driving force for the observed exchange of organic groups between benzylpalladium halides and *p*-tolylmagnesium and -zinc halides is likely the greater thermodynamic stability of the more stable benzyl anion bound to the more electropositive metal (Mg, Zn) and the sp^2 C atom (*p*-Tol) bound to the palladium, in agreement with the fact that no exchange is observed between *p*-tolylpalladium halides and benzylmagnesium or -zinc halides. The mechanism by which the exchange reaction occurs was not investigated, but likely mechanisms are similar to those proposed for other alkyl group transfer reactions observed between different platinum or palladium centers or in transmetalation reactions.[30–32] Possible intermediates, including dinuclear complexes and an anionic five-coordinate palladium complex, are shown in Scheme 3. The reactions might be preceded by halide dissociation as was proposed for the alkyl group transfer between a Pd(IV) and a Pt(II) complex.[32] Dissociation of one of the coordinating N atoms, similar to the initial loss of a neutral ligand reported for reactions involving palladium/platinum complexes containing monodentate phosphine or sulfide ligands,[30,31] is unlikely due to the rigidity of the naphthalene backbone. The fact that no exchange is observed between benzylpalladium and *p*-tolyltin reagents can be ascribed to the much slower formation of intermediates such as in Scheme 3 in the case of tin reagents, relative to the rate of formation of intermediates which lead to transmetalation and formation of diorganopalladium(II) complex.

Further evidence for the proposed mechanism of formation of homocoupled products comes from reactions with organotin reagents. The reaction of $\mathrm{PdBr(CH_2Ph)}$(*p*-Tol-BIAN) with $\mathrm{SnMe_4}$ led to the formation of PdBrMe(*p*-Tol-BIAN) and $\mathrm{PhCH_2SnMe_3}$ (Scheme 2), and in the Pd(Ar-BIAN)-catalyzed coupling of benzyl bromide

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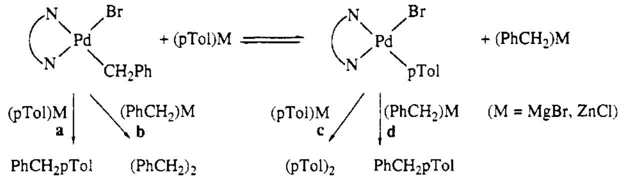
Scheme 4



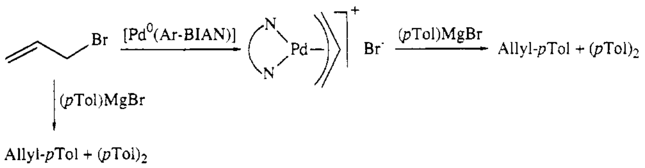
with tetramethyltin, 10% bibenzyl was formed.[10e,f] On the contrary, in the carbonylative coupling of benzyl bromide with tetramethyltin, no formation of bibenzyl was observed,[10e,f] and in the reaction of $PdBr(C(O)CH_2Ph)$(*p*-Tol-BIAN) with $SnMe_4$, no exchange of organic groups occurred (Scheme 2).

Exchange of organic groups between palladium and a transmetalating reagent has been observed previously[28,33] and has been described to explain the formation of homocoupled products in Pd-catalyzed cross-coupling reactions of, e.g., aryl iodides with aryl- and vinylmagnesium compounds, although convincing experimental evidence for such a mechanism has not been presented.[11f,h–k] Formation of homocoupled products via an exchange of organic groups prior to C–C coupling is further supported by the fact that several other mechanisms, which could in principle lead to the formation of homocoupled products, could all be excluded on the basis of our experimental data (vide infra).

After exchange of the organic group between palladium and the transmetalating reagent, a mixture of two organopalladium(II) complexes and two transmetalating reagents is formed, which can combine in four different ways leading to the formation of either cross-coupled or homocoupled products (Scheme 4). The outcome of a certain reaction is dependent on the relative rates of the different combination reactions a–d, which in turn depend on the organic halide and the transmetalating reagent used. For example, in the coupling reaction of benzyl bromide with *p*-tolylmagnesium bromide, after benzyl/*p*-tolyl exchange, a mixture of benzylpalladium, *p*-tolylpalladium, benzylmagnesium, and *p*-tolylmagnesium compounds is formed. The formation of mainly homocoupled products must be attributed to the much faster reactions of the benzylpalladium complex with benzylmagnesium bromide (b) and of the *p*-tolylpalladium complex with *p*-tolylmagnesium bromide (c) as compared to the two other possible combinations a and d. Alternatively, some direct reaction between benzyl bromide and benzylmagnesium bromide might contribute to the formation of bibenzyl. The higher rate of the reaction of *p*-tolylpalladium complexes with *p*-tolylmagnesium bromide as compared to benzylmagnesium bromide also appeared from the coupling of *p*-tolyl bromide with these reagents (Table 1). In the coupling of benzyl bromide with *p*-tolylzinc chloride instead of *p*-tolylmagnesium bromide, some cross-coupled product is formed, indicating that in this case, after exchange of organic groups, the cross-coupling reactions (a and d) compete with the homocoupling reactions (b and c).

Coupling Reactions with Allylic Halides. More support for the exchange mechanism, which accounts for the formation of homocoupled products, stems from the cross-coupling reactions of allyl bromide with *p*-tolylmagnesium bromide. In the presence of a Pd(Ar-BIAN) catalyst the amount of homocoupling has increased as compared to the uncatalyzed reaction, indicating that the palladium center plays an important role in the formation of homocoupled products. The possibility of exchange of organic groups between allylpalladium complexes and transmetalating reagents appeared from the reaction of [Pd(η^3-allyl)(*p*-Tol-BIAN)]Br with *p*-tolylmagnesium bromide at −70 °C, which led to the formation of PdBr(*p*-Tol)(*p*-Tol-BIAN) and $(p\text{-Tol})_2$, among other products.

Scheme 5



In the Pd(Ar-BIAN)-catalyzed coupling reaction there are two competing pathways: reaction of the allyl bromide directly with *p*-tolylmagnesium bromide and reaction with the palladium complex, followed by reaction of the complex with *p*-tolylmagnesium bromide (Scheme 5). As the uncatalyzed reaction proceeds efficiently, the reaction of the allylic halide with the Pd(Ar-BIAN) complex has to be fast in order to compete effectively with the direct coupling. Studies of the oxidative addition of allylic halides to Pd(Ar-BIAN)(alkene) complexes have revealed that the rate of oxidative addition decreased with increasing steric bulk of the aromatic group on the imine N atom, i.e., the rate decreased in the order $C_6H_5 \approx p\text{-}MeC_6H_4 > o\text{-}MeC_6H_4 > o,o'\text{-}i\text{-}Pr_2C_6H_3$.[27] In agreement with this observation, the product distribution of the Pd(Ar-BIAN)-catalyzed allyl coupling reactions changes toward that of the uncatalyzed reaction in the same order.

An increase in the concentration of the $PdCl_2$(Ph-BIAN) catalyst from 1 to 5% has only a slight influence on the product distribution, indicating that the product distribution is determined by the Pd(Ph-BIAN)-catalyzed coupling alone and not by a combination of direct and Pd-catalyzed reactions. Thus, in the case of a $PdCl_2$(Ph-BIAN) catalyst, reaction of the allyl bromide with the Pd complex is much faster than direct reaction with *p*-tolylmagnesium bromide. The observation that the amount of bi-*p*-tolyl increases by using 5% $PdCl_2$(*o*-Tol-BIAN) as catalyst, instead of 1%, indicates that the contribution from the palladium-catalyzed coupling becomes more important with increasing catalyst concentration, in agreement with a competition between direct reaction and a palladium-catalyzed reaction of allyl bromide with *p*-tolylmagnesium bromide in the case of the bulky Ar-BIAN ligands.

Exclusion of Other Possible Pathways Leading to Homocoupled Products. Studies on palladium–phosphine-catalyzed coupling reactions and studies on the mechanism of reductive elimination from organopalladium(II) complexes have revealed several mechanisms, which must be taken into account for the explanation of homocoupled products in cross-coupling reactions. These mechanisms, including (i) halogen–metal exchange between the organic halide and the transmetalating reagent, (ii) reductive elimination from a palladium(IV) or (iii) from a dinuclear palladium(II) complex, (iv) reactions via radical mechanisms, and (v) disproportionation reactions, have all been excluded on the basis of our experimental observations, as will be described below.

In the first place halogen–metal exchange could occur (cf. eq 2), as has been observed in some reactions of organic halides with transmetalating reagents. This mechanism is often used to explain the formation of homocoupled products in palladium–phosphine-catalyzed reactions.[11]

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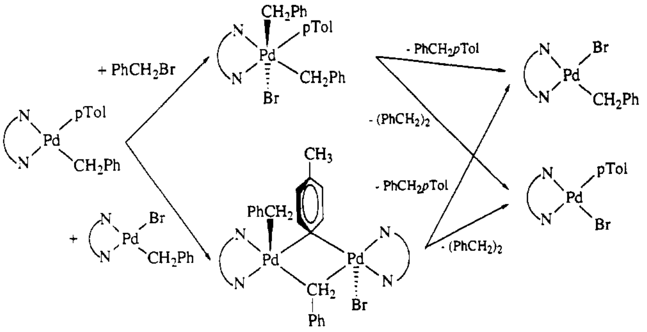
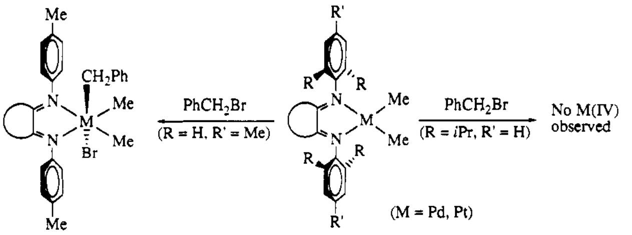
Scheme 6



Scheme 7



However, this exchange is not observed in the reaction of benzyl bromide with *p*-tolylzinc chloride in the absence of a Pd(Ar-BIAN) catalyst within 2 h at 20 °C, whereas in the Pd(Ar-BIAN)-catalyzed reaction at 20 °C homocoupled products are formed within the period of 1 h for the reaction to go to completion (by using 1% catalyst). Furthermore, halogen–metal exchange would lead to formation of *p*-bromotoluene, which is never observed in the product at any stage of the reaction. Separate experiments showed that *p*-bromotoluene reacted slowly with benzylmagnesium bromide and *p*-tolylmagnesium bromide in the catalytic coupling (Table 1), and it is thus impossible that significant amounts of free *p*-bromotoluene are formed during the coupling reaction, which is generally completed within 1 h. These results indicate that halogen–metal exchange between the organic halide and the transmetalating reagent cannot play a significant role in the Pd(Ar-BIAN)-catalyzed coupling of benzyl bromide with *p*-tolylmagnesium or *p*-tolylzinc reagents.

Another possibility to explain the formation of homocoupled products can be derived from the mechanism by which reductive elimination occurs after the transmetalation step. From studies on the reductive elimination from diorgano–bis(phosphine)palladium(II) complexes, two mechanisms have been proposed which might play a role in catalytic cross-coupling reactions. After the transmetalation, either the diorgano–Pd(II) species formed undergoes a further oxidative addition, to give a triorgano–Pd(IV) species from which reductive elimination occurs,[13a,28] or the diorgano–Pd(II) complex associates with an organo–Pd(II) halide, giving a dinuclear species from which reductive elimination occurs.[34] Extending these mechanisms to the Pd(Ar-BIAN)-catalyzed coupling of benzyl bromide with *p*-tolylmetal reagents gives the two possibilities for reductive elimination after formation of a transient $Pd(CH_2Ph)(p\text{-}Tol)$(Ar-BIAN) species (Scheme 6). Reductive elimination from these intermediates can give either cross coupling ($PhCH_2$-*p*-Tol) or homocoupling ($PhCH_2CH_2Ph$). The palladium complexes then formed again react with benzyl bromide or *p*-TolM (M = MgBr, ZnCl, or SnR_3), resulting in the formation of $PhCH_2$-*p*-Tol, $PhCH_2CH_2Ph$, or $(p\text{-}Tol)_2$ in a subsequent step.

If the intermediacy of a palladium(IV) species were important for the formation of homocoupled products, it is expected that the amount of homocoupled products would decrease when the steric hindrance around the palladium center is increased. Reaction of benzyl bromide with $PdMe_2(o,o'\text{-}i\text{-}Pr_2C_6H_3$-BIAN) was much slower (1.5–5 h) than the instantaneous formation of $Pd^{IV}BrMe_2(CH_2Ph)$(Ar-BIAN) upon addition of benzyl bromide to $PdMe_2$(*p*-Tol-BIAN) (the same observations were made for the analogous $PtMe_2$(Ar-BIAN) complexes, Scheme 7).[35] The isopropyl substituents of the $o,o'\text{-}i\text{-}Pr_2C_6H_3$-BIAN ligand cause severe steric hindrance around the palladium center due to the orientation of the aromatic ring almost perpendicular to the coordination plane,[18,36] hindering approach of substrates from axial positions. As the $PdCl_2(o,o'\text{-}i\text{-}Pr_2C_6H_3$-BIAN)-catalyzed cross coupling of benzyl bromide with *p*-tolylzinc chloride did not lead to a decrease in the amount of homocoupled products (Table 1), it can be concluded that palladium(IV) intermediates do not play a significant role in the formation of homocoupled products. Thus, reductive elimination in the Pd(Ar-BIAN)-catalyzed coupling reactions occurs from a palladium(II) complex, in agreement with the described facile reductive elimination from diorgano–palladium(II) complex containing at least one Pd–C(sp^2) bond.[33,37]

Formation of a dinuclear complex from which reductive elimination occurs seems very unlikely: if the ratio of cross coupling to homocoupling were determined by such a dinuclear species, the tremendous influence of the transmetalating reagent could not be explained. Furthermore, formation of such a dinuclear complex is suggested to involve a tricoordinate $Pd(L)Ar_2$ species,[34] which can be formed easily by dissociative loss of one (phosphine) ligand from the $Pd(L)_2Ar_2$ complex when monodentate or flexible bidentate ligands are coordinated to the palladium. In the case of Pd(Ar-BIAN) complexes with the rigidly chelating Ar-BIAN ligand, a dinuclear complex with two axial ligands should be formed, which seems to be very unlikely, especially if a sterically hindered $o,o'\text{-}i\text{-}Pr_2C_6H_3$-BIAN ligand with large ortho substituents on the aromatic group is used. As the Pd(Ar-BIAN)-catalyzed reaction yields the same product distribution, irrespective of the use of either sterically hindered or unhindered ligands coordinated to the palladium, such a mechanism via dinuclear complexes cannot be involved.

A fourth way to explain the formation of homocoupled products is by the disproportionation of $PdBr(CH_2Ph)$(Ar-BIAN) (eq 6), analogous to the formation of coupling products R_2 from the monoorgano nickel complexes $Ni(R)X(L)_2$, as was described for $Ni(Ph)Cl(PPh_3)_2$,[38] $Ni(Me)(acac)(PPh_3)$[39] (acac = acetylacetonato), $Ni(C_2H_5)Cl(bpy)$,[40] and NiBr(Ph)(bpy).[41] After disproportionation, reductive elimination from $Pd(CH_2Ph)_2$(Ar-BIAN) would

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[34] (a) Ozawa, F.; Fujimori, M.; Yamamoto, T.; Yamamoto, A. *Organometallics* **1986**, *5*, 2144. (b) Ozawa, F.; Hidaka, T.; Yamamoto, T.; Yamamoto, A. *J. Organomet. Chem.* **1987**, *330*, 253.

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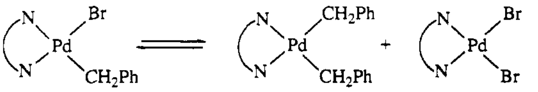
lead to bibenzyl and reaction of $PdBr_2$(Ar-BIAN) with *p*-TolMgBr followed by reductive elimination to $(p\text{-Tol})_2$.



(6)

In our case the amount of disproportionation can be neglected, because it was shown that in THF at 20 °C $PdBr(CH_2Ph)$(*p*-Tol-BIAN) did not give any $PhCH_2CH_2Ph$ within 2 h, which is long compared to the time scale of the catalytic reaction. In a similar reaction the aryl complex Pd(*p*-Tol)I(*p*-Tol-BIAN) was shown to be stable toward disproportionation in THF for at least 2 h at 20 °C.

A fifth reaction pathway that could lead to the formation of homocoupled products is the occurrence of a free radical mechanism. The formation of radicals can occur in the oxidative addition of benzyl bromide to Pd (radical mechanisms in oxidative addition have been well documented[42]) or upon charge-transfer interactions between a Pd(II) complex and the transmetalating reagent,[42] after which radicals can be formed from the radical pair $[PdBr(CH_2Ph)(Ar\text{-}BIAN)^{\bullet -}[p\text{-}TolM]^{\bullet +}$. However, styrene and *m*-dinitrobenzene did not influence the product distribution or the rate of the coupling reaction and, in the presence of styrene, no products arising from coupling of radicals with styrene were observed; hence the formation of free radicals in the catalytic coupling reaction can be excluded.

Comparison with Palladium–Phosphine Catalysts. When a palladium–phosphine catalyst such as $PdCl_2(PPh_3)_2$ or $PdCl_2$(dppe) is used to catalyze the reaction of benzyl bromide with *p*-tolylmagnesium bromide, the reaction becomes about 2–3 orders of magnitude slower (Table 2), but a higher selectivity for cross coupling is observed (30%) as compared to similar Pd(Ar-BIAN)-catalyzed reactions (7–9%). The higher rate of the Pd(Ar-BIAN)-catalyzed reaction as compared to the Pd–phosphine-catalyzed reaction reflects the increased reactivity of Pd(Ar-BIAN) complexes toward oxidative addition, which was shown to be the rate-determining step.

One reason for the increased amount of homocoupling in Pd(Ar-BIAN)-catalyzed reactions may be the difference in geometry between the organopalladium complexes formed after oxidative addition when comparing the bis(monophosphine) and the Ar-BIAN palladium complexes; oxidative addition of $PhCH_2Br$ to $Pd(PPh_3)_2$ leads to a *trans*-$PdBr(CH_2Ph)(PPh_3)_2$ complex, whereas $PdBr(CH_2Ph)$(Ar-BIAN) has a *cis* geometry enforced by the chelating coordination of the Ar-BIAN ligand. For the *trans* organopalladium–phosphine complex the rate of bromide substitution is enhanced as compared to the *cis*-Pd(Ar-BIAN) complex due to the larger *trans* effect of the benzyl ligand than the imine N atom, leading to faster substitution and less concurring exchange of organic groups between palladium and the transmetalating agent, and hence to an increased amount of cross-coupled product. For phosphine complexes of the type *cis*-$PdBr(CH_2Ph)$(dppe), transmetalation will be fast due to the larger *trans* influence of P as compared to N in the $PdBr(CH_2Ph)$(Ar-BIAN) complexes. The lower amounts of homocoupled products as reported for systems containing chelating diphosphines as compared to those containing monophosphines[11h-k] may be due to the fact that no isomerization to *cis* complexes is required in the case of the former.

Conclusion

The use of palladium complexes containing Ar-BIAN ligands in catalytic carbon–carbon bond forming reactions, instead of the more commonly used phosphines, has allowed us to investigate viable mechanisms leading to the formation of homocoupled products. The use of Ar-BIAN ligands in the catalytic system appears to be very useful for mechanistic studies, because the substituents on the imine N atom can easily be varied and the influence of these substituents on both catalytic and stoichiometric reactions can be systematically evaluated.

We have shown by a detailed and systematic study of the coupling reaction of benzyl bromide with *p*-tolylmagnesium, -zinc, and -tin reagents that the formation of homocoupled products arises, at least in that case, by facile exchange of organic groups between the transmetalating reagent and the organopalladium complex formed after oxidative addition of the organic halide. Possibly, this mechanism is not limited to the Pd-catalyzed coupling reaction of benzyl bromide with *p*-tolylmetal species, but is also applicable to such reactions involving other coupling partners, such as allyl bromide and *p*-tolylmagnesium bromide.

The exchange of organic groups between an organopalladium complex and a transmetalating reagent is not restricted to Pd(Ar-BIAN) complexes and has been observed also in the reactions of *trans*-$Pd(CH_2Ph)X(PPh_3)_2$ (X = Cl, Br) with $SnMe_4$ or methylmagnesium bromide[28] and in the reaction of *cis*- and *trans*-diorganopalladium(II)bis(diethylphenylphosphine) complexes with organomagnesium compounds (eq 7).[33]

$$Pd(Me)(Ph)(PEt_2Ph)_2 \underset{PhMgI}{\overset{MeMgI}{\rightleftharpoons}} PdMe_2(PEt_2Ph)_2 \qquad (7)$$

As formation of homocoupled products is observed in the $Pd(PPh_3)_n$-catalyzed reaction of benzyl chloride with methylmagnesium bromide (where mainly bibenzyl is formed)[11l] and in the $Pd(PEt_2Ph)_n$-catalyzed reaction of iodobenzene with methylmagnesium iodide (6% biphenyl is formed),[33] these products may arise by the mechanism proposed in Scheme 4. Such a mechanism had in fact been proposed, although not unambiguously proven, to occur for a variety of other Pd-catalyzed cross-coupling reactions, e.g., reactions of aryl halides with arylmagnesium and vinylmagnesium reagents.[11h-k]

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