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Palladium Complexes Containing Rigid Bidentate Nitrogen Ligands as Catalysts for Carbon-Carbon Bond Formation [1]

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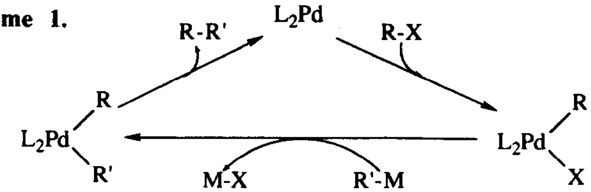
Abstract: Zerovalent Pd(Ar-BIAN)(dimethyl fumarate) and divalent $PdCl_2$(Ar-BIAN) complexes containing the rigid bidentate nitrogen ligand bis(arylimino)acenaphtene (Ar-BIAN; Ar = C_6H_5, *p*-MeC_6H_4, *p*-$MeOC_6H_4$) are efficient catalysts for the cross coupling reaction of various organic halides (including acyl-, allyl-, aryl-, benzyl-, vinyl- and 1,2-dienylhalides) with organomagnesium, -zinc and -tin reagents. Coupling reactions of organic halides with one equivalent of organomagnesium and -zinc reagents, in the presence of 1 mol % of a Pd(Ar-BIAN) catalyst, generally proceed smoothly in THF at 20 °C, giving complete conversion of the starting halide within 1-16 hours. Good isolated yields of carbon-carbon coupled products are obtained and the ratio cross/homo coupling varies between 98/2 and 0/100, depending on the substrates used. Reactions employing organotin reagents proceed best in DMF or HMPA and need longer reaction times and/or higher temperatures, as compared to organomagnesium and -zinc reagents, to go to completion. The selectivity for cross coupling is high (generally >99 %) and high isolated yields of cross coupled products can be obtained. In the presence of carbon monoxide (1-5 bar) ketones can be formed with excellent selectivity and in good yields, as was demonstrated for the carbonylative coupling of benzyl bromide with tetramethyltin or (*p*-tolyl)trimethyltin. Comparison of some Pd(Ar-BIAN) catalyzed reactions with Pd-phosphine catalyzed reactions reveals that these reactions complement each other: for example, when a Pd(Ar-BIAN) catalyst was employed, the coupling of 2-methylallyl chloride with phenyltributyltin was much faster, whereas the coupling of iodobenzene with vinyltrimethyltin was much slower, as compared to the $Pd(PPh_3)_n$ catalyzed reactions.

INTRODUCTION

The palladium catalyzed cross coupling reaction has become a versatile tool in organic synthesis and a wide variety of organic electrophiles and trans metallating reagents can be used[2]. The separate steps that occur in the catalytic coupling (scheme 1), are strongly dependent on the type of ligands coordinated to the metal centre[3]. However, little attention has been directed to the influence of the ligands coordinated to the palladium centre on the catalytic reaction.

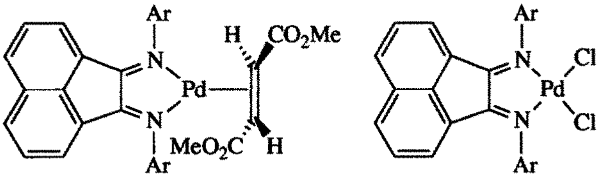
Scheme 1.



Sofar, in catalytic reactions, mainly monodentate phosphine complexes of palladium have been employed. Complexes containing bidentate chelating phosphine ligands are efficient catalysts for Grignard cross coupling reactions[2a], but for cross coupling reactions employing organotin compounds both decreased[4] and increased[5] rates have been reported.

The few reports dealing with carbon-carbon bond formation catalyzed by palladium complexes of bidentate nitrogen ligands include nucleophilic allylic substitution[6] and coupling reactions of organic halides with organotin reagents catalyzed by Pd(2,2'-bipyridine)[7], or Pd(bis(2-pyridyl) silane)[8]. Stoichiometric formation of a carbon-carbon coupled product from various Pd(η^3-allyl)(α-diimine) complexes[9] and (isolated) Pd(IV) complexes[10] has also been reported.

We describe here several examples of Pd(Ar-BIAN) catalyzed cross coupling reactions under mild conditions, catalyzed by Pd(Ar-BIAN)(dmfu) (dmfu = dimethyl fumarate) and $PdCl_2$(Ar-BIAN) complexes, i.e. complexes containing the rigid bidentate nitrogen ligands bis(arylimino) acenaphthene (Ar = C_6H_5, *p*-$CH_3C_6H_4$, *p*-$CH_3OC_6H_4$). Part of this work has been published as a preliminary communication[11].



Ar = C_6H_5
p-MeC_6H_4
p-$MeOC_6H_4$

We expected these ligands to endow properties upon the palladium centre which might be favourable in such reactions. Because of their good σ-donor and π-acceptor capacities, both higher and lower oxidation states, necessary in an alternating sequence of oxidative addition and reductive elimination, can be stabilized. Furthermore, due to the chelating coordination of the *cis* fixed Ar-BIAN ligand, the diorganopalladium(II) complex formed after transmetallation has both organic groups in a *cis* orientation, facilitating reductive elimination from this type of complexes. Apart from anticipated behaviour it has appeared, to our surprise, that zerovalent Pd(Ar-BIAN)(alkene) complexes are also active as catalysts in the homogeneous hydrogenation of electron poor alkenes[12].

EXPERIMENTAL

All reactions were performed in an atmosphere of dry nitrogen using standard Schlenk techniques. All solvents were carefully dried and distilled prior to use, except hexamethylphosphorous triamide (HMPA), which was used as received. ^1H NMR spectra were recorded on a Bruker AC 100 spectrometer (100.13 MHz), relative to tetramethylsilane as external standard and IR spectra on a Perkin Elmer 283 spectrophotometer. 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) and GCMS on a Hewlett-Packard 5890 series II gas chromatograph with a Gerstel CIS III temperature controlable injector, a HP 5971-A mass selective detector, with electron impact ionization at 70 eV, and a HP Ultra-2 column (length 25 m, 0.20 mm inner diameter, 0.33 μm film thickness). $PhCH_2MgCl$[13], $CH_2{=}CHSnMe_3$[14], $Pd(DBA)_2$[15], Ar-BIAN[16], Pd(Ar-BIAN)(dmfu)[17] and $PdCl_2$(Ar-BIAN)[18] were synthesized following reported procedures. Other organomagnesium reagents were synthesized by standard procedures[19] and titrated with a 0.500 M 2-butanol solution in xylene against a phenanthroline indicator[20]. Organotin reagents were synthesized via standard procedures, from the reaction of the trialkyltinchloride with a slight excess of organomagnesium or organolithium compounds[21]. Organic coupling products were characterized by ^1H NMR, GC/GCMS and IR and were compared with authentic samples.

Coupling reactions with organomagnesium reagents. To a solution of 13.7 mg $PdCl_2$(Ph-BIAN) (0.027 mmol) in 20 ml THF was added 0.30 ml iodobenzene (2.7 mmol), followed by 9.0 ml of a 0.319 M benzyl magnesium chloride solution in THF (2.9 mmol). The solution was stirred at 20 °C and after 16 hours 30 ml of water was added. The organic products were extracted from the reaction mixture with petroleum ether 40-60 (3 x 30 ml). The organic layer was back extracted with brine (20 ml), dried on $MgSO_4$ and evaporated to dryness. The organic product was purified by chromatography over silica, using 100 ml petroleum ether 40-60 as eluent. The colorless fraction was evaporated to dryness and the product dried in vacuo giving 0.45 g of a white pasty product (99 %). Other reactions were carried out in a similar way (table 1).

Coupling reactions with organozinc reagents. To 2.0 ml 1.0 M $ZnCl_2$ solution in diethyl ether and 10 ml THF, cooled to 0 °C in ice/water, was added dropwise 4.2 ml of a 0.473 M *p*-tolyl magnesium bromide solution in THF (2.0 mmol). After the mixture was stirred at 0 °C for 1 hour, the icebath was removed and 0.25 ml *E*-β-bromostyrene (1.94 mmol) was added, followed by 10.2 mg $PdCl_2$(Ph-BIAN) (0,020 mmol). The mixture was heated to reflux and stirred at that temperature for 2 hours. Then 30 ml dilute hydrochloric acid was added and the mixture extracted with hexane (3 x 30 ml). The combined organic layers were backextracted with water (30 ml) and a 10 % K_2CO_3 solution in water (30 ml), dried on $MgSO_4$, filtered and evaporated to dryness. Purification was achieved by chromatography over silica (150 ml hexane). The colorless fraction was evaporated to dryness and the product dried in vacuo giving 342 mg of a white solid (98 %).

Coupling reactions with organotin reagents. *Method A*. To a solution of 11.7 mg Pd(Ph-BIAN)(dmfu) (0.020 mmol) in 15 ml DMF were added 0.23 ml benzyl bromide (1.94 mmol) and 0.40 ml tetramethyltin (2.89 mmol). The flask was closed and the mixture stirred at 50 °C. After 20 hours the mixture was cooled to 20 °C and 0.30 ml n-octane was added (1.84 mmol; internal GC standard), followed by 20 ml water. The organic products were extracted from the aqueous layer with pentane (3 x 30 ml). The combined pentane fractions were backextracted with water (2 x 20 ml) and brine (20 ml). One ml of this solution was filtered through neutral alumina for GC. The rest of the solution was dried on $MgSO_4$, filtered and evaporated at 0 °C, leaving behind a colorless liquid. Other reactions were carried out in a similar way (table 2).

Method B. To a solution of 11.8 mg $Pd(DBA)_2$ (0.0205 mmol; DBA = dibenzylideneacetone) in 20.5 ml THF was added 7.4 mg *p*Tol-BIAN (0.0205 mmol) and the mixture stirred at 20 °C. After 15 minutes 0.24 ml benzoyl chloride (2.07 mmol) and 0.52 g (2-furyl)trimethyltin (2.25 mmol) were added and the mixture heated to reflux. At certain intervals aliquots were removed from the reaction mixture and the progression of the reaction monitored (by ^1H NMR, IR and GC/GCMS).

Carbonylative cross coupling reactions. In a Schlenk tube of 500 ml were put together 10 ml HMPA, 9.8 mg Pd(Ph-BIAN)(dmfu) (0.017 mmol), 0.19 ml benzyl bromide (1.60 mmol) and 0.25 ml tetramethyltin (1.80 mmol) and the flask was sealed with a septum. The flask was evacuated and carbon monoxide gas was admitted up to a pressure of 1.1 bar. This evacuation/CO inlet sequence was repeated twice, after which the flask was closed and the mixture stirred at 20 °C. After 20 hours the flask was opened and 0.30 ml n-octane added (1.84 mmol), followed by 20 ml water. Workup was carried out as described above (method A). Chromatography on silica with hexane/diethyl ether (1 : 1 v/v) yielded the pure product as a colorless liquid (0.19 g, 88 %).

Carbonylative coupling of benzyl bromide with (*p*-tolyl)trimethyltin was carried out in DMF at 50 °C under 5 bar CO in an autoclave.

Heck-type reactions. To 11.0 mg Pd(Ph-BIAN)(dmfu) (0.019 mmol) in 10 ml DMF were added 0.32 g *p*-iodotoluene (1.47 mmol), 0.22 ml styrene (1.92 mmol) and 0.30 ml triethylamine (2.16 mmol). The mixture was stirred at 50 °C for 4 hours and subsequently cooled to 20 °C. Water (20 ml) was added and the mixture was extracted with diethyl ether (3 x 30 ml). The combined organic layers were backextracted with water (2 x 30 ml) and brine (20 ml), dried on $MgSO_4$ and filtered. After evaporation the product was obtained as a pasty solid. ^1H NMR spectroscopy showed the presence of *E*-PhCH=CH(*p*Tol). Reactions of *p*-iodotoluene with methylacrylate and of iodobenzene with cyclopentene were carried out in the same way.

Table 1. Pd(Ar-BIAN) Catalyzed Cross Couping of Organic Halides with Organomagnesium and Zinc Reagents[a].

Organic halide	Mg/Zn reagent	Conditions	Products[b]	yield[c]
*p*Tol-I	$PhCH_2MgCl$	20 °C, 16 h	(*p*Tol)CH_2Ph (98 %) + $(PhCH_2)_2$ (2 %)	85
Ph-I	$PhCH_2MgCl$	20 °C, 16 h	$PhCH_2Ph$ (98 %) + $(PhCH_2)_2$ (2 %)	99
PhCH=CHBr	*p*TolMgBr	67 °C, 2 h	PhCH=CH(*p*Tol) (67 %) + $(p\mathrm{Tol})_2$ (33 %)	99
PhCH=CHBr	*p*TolZnCl	67 °C, 2 h	PhCH=CH(*p*Tol) (88 %) + $(p\mathrm{Tol})_2$ (12 %)	98
$Me_2C{=}C{=}CHBr$	*p*TolMgBr	20 °C, 2 h	$Me_2C{=}C{=}CH$(*p*Tol) (64 %) + $(p\mathrm{Tol})_2$ (36 %)	49
$Me_2C{=}C{=}CHBr$	*p*TolZnCl	20 °C, 3 h	$Me_2C{=}C{=}CH$(*p*Tol) (77 %) + $(p\mathrm{Tol})_2$ (23 %)	66
$Me_2C{=}C{=}CHBr$	$PhCH_2MgCl$	20 °C, 2.5 h	$Me_2C{=}C{=}CH(CH_2Ph)$ (98 %) + $(PhCH_2)_2$ (2 %)	n.d.
PhCH(Me)Br	AllylMgCl	20 °C, 2 h	PhCH(Me)-Allyl (85 %) + $(PhCH(Me))_2$ (15 %)	88
PhCH(Me)Br	$PhCH_2MgCl$	20 °C, 16 h	$(PhCH(Me))_2$ (44 %) + $(PhCH_2)_2$ (56 %)	n.d.
$PhCH_2Br$	AllylMgCl	20 °C, 4 h	$(PhCH_2)_2$ (no $PhCH_2$-Allyl)	n.d.

[a] 1 mol % Pd(Ar-BIAN)(dimethyl fumarate) or $PdCl_2$(Ar-BIAN) was used as catalyst (generally Ar = Ph, *p*Tol) and conversion was complete within the indicated time, unless noted otherwise. Abbreviations used: Ph = C_6H_5, *p*Tol = *p*-MeC_6H_4, Allyl = CH_2-CH=CH_2, Me = CH_3, n.d. = not determined. [b] The relative amounts of the products in the crude reaction mixture (i.e. before chromatographic workup) are indicated in parentheses. [c] Total yield (in %, based on the starting halide) of the organic product(s) after chromatographic workup.

RESULTS

Cross coupling with organomagnesium and -zinc reagents

The cross coupling reaction between organic halides and organomagnesium and -zinc reagents readily takes place in THF at 20 °C and conversion of the halide is generally complete within several hours employing 1 % of Pd(Ar-BIAN) catalyst, except for aryl iodides which require reaction overnight to go to completion. Both zerovalent Pd(Ar-BIAN)(dmfu) (dmfu = dimethyl fumarate) and divalent $PdCl_2$(Ar-BIAN) are active as catalyst. For the various Ar-BIAN ligands containing phenyl, *p*-tolyl or *p*-methoxyphenyl substituents, there is no difference either in the rate of the coupling reaction or the product distribution[22]. Yields of isolated products after chromatographic workup are good (85-99 %), except for 1,2-dienyl bromides which give only 49-66 % yield.

The results, summarized in table 1, clearly indicate that the ratio cross/homo coupling strongly depends on the reagents. Aryl iodides reacted with benzyl magnesium chloride to give the cross coupled products almost exclusively, whereas benzyl bromide reacted with *p*-tolyl magnesium bromide to give almost exclusively homocoupled products[23]. Benzyl bromide led in a very facile way to homocoupled product in the reaction with organomagnesium halides, as was also clear from the exclusive formation of bibenzyl in the reactions with methyl magnesium iodide, dimethyl magnesium and allyl magnesium chloride (in these cases some reaction was observed in the absence of catalyst, but these were much slower than the Pd(Ar-BIAN) catalyzed reactions). Coupling reactions of 1-phenylethyl bromide with organomagnesium reagents produced only trace amounts of 1 % styrene, indicating that transmetallation is fast compared to β-elimination: with allyl magnesium chloride predominantly cross coupled product was formed, whereas with benzyl magnesium chloride exclusively homocoupled bibenzyl and 2,3-diphenyl-butane (a 1 : 1 mixture of *rac* and *meso*) were formed. *E*-β-bromostyrene reacted with *p*-tolyl magnesium bromide in refluxing THF to give the substituted stilbene derivative as the main reaction product together with a considerable amount of homocoupled bi-*p*-tolyl. In the latter case no cross coupling occurred in the absence of the Pd(Ar-BIAN) catalyst, but then about 35 % bi-*p*-tolyl was formed.

When organozinc reagents are used in the cross coupling reactions, instead of organomagnesium reagents, the amount of homocoupling is considerably lower than in comparable reactions with organomagnesium reagents, as was shown by the reactions of *E*-β-bromostyrene and 1-bromo-3-methyl-1,2-butadiene with *p*-tolyl zinc chloride.

Table 2. Pd(Ar-BIAN) Catalyzed Cross Coupling of Organic Halides with Organotin Reagents[a].

Organic halide	Sn reagent [b]	Conditions[c]	Products [d]	Yield[e]
$PhCH_2Br$	$SnMe_4$	A, B, 20 h	$PhCH_2CH_3$ (90 %) + $(PhCH_2)_2$ (10 %)	84 [f]
$PhCH_2Br$	*p*$TolSnR_3$	A, B, 20 h	$PhCH_2$*p*Tol (> 99 %)	76
$PhCH_2Br$	$PhSnMe_3$	A, 24 h	$PhCH_2Ph$ (> 99 %)	80 [f]
AllylBr	*p*$TolSnR_3$	A, 16 h	*p*Tol-CH_2-CH=CH_2 (> 99 %)	88
2-MeallCl	$PhSnBu_3$	A, 1 h	Ph-CH_2-C(Me)=CH_2 (> 99 %)	92 [f]
2-MeallCl	*p*$TolSnR_3$	A, 16 h	*p*Tol-CH_2-C(Me)=CH_2 (> 99 %)	90
*p*Tol-I	$SnMe_4$	A, 18 h	*p*Tol-Me (41 %) + *p*Tol-I (59 %) [g]	n.d.
*p*Tol-I	*p*$TolSnBu_3$	A, 18 h	$(p\text{Tol})_2$ (35 %) + *p*Tol-I (65 %)	n.d.
Ph-I	CH_2=$CHSnMe_3$	A, 16 h [h]	Ph-CH=CH_2 (49 %) + Ph-I (51 %)	n.d.
PhC(O)Cl	$SnMe_4$	A, 16 h	PhC(O)Me (> 99 %)	98
MeC(O)Cl	$PhSnMe_3$	A, 15 h	PhC(O)Me (> 99 %)	n.d.
EtC(O)Cl	*p*$TolSnR_3$	A, 17 h	*p*TolC(O)Et (> 99 %)	85
PhC(O)Cl	$FurSnMe_3$	THF, 3 h [i]	PhC(O)-Fur (71 %) + Fur_2 (14 %) + $(PhC(O))_2$ (15 %)	75 [f]
$PhCH_2Br$	$SnMe_4$	B, CO, 20 h	$PhCH_2C(O)Me$ (> 99 %)	88
$PhCH_2Br$	*p*$TolSnBu_3$	A, CO, 15 h	$PhCH_2C(O)$*p*Tol (> 99 %)	79

[a] Unless noted otherwise, conversion was complete within the indicated time when 1 mol % of a Pd(Ar-BIAN) (dimethyl fumarate) catalyst was employed (generally Ar = Ph, *p*Tol). Abbreviations used: Bu = $(CH_2)_3CH_3$, 2-Meall = CH_2-C(Me)=CH_2, Fur = C_4H_3O (2-furyl), see also table 1. [b] R = Me, Bu. [c] A: in DMF at 50 °C; B: in HMPA at 20 °C. The reactions were usually carried out overnight to ensure complete conversion of the starting halide and the conditions were not optimized. [d] The relative amounts of the product in the crude reaction mixture, before chromatographic workup, are shown in parentheses. [e] Total yield of the organic product(s) after chromatographic workup. [f] GC yield. [g] Complete conversion was achieved within 24 h in HMPA at 20 °C using 2 mol % of catalyst. [h] 2 mol % of catalyst. [i] In THF at 67 °C (reflux temperature), employing a catalyst prepared in situ from 1 mol % $Pd(dba)_2$ and 5 mol % *p*Tol-BIAN (75 % conversion of PhC(O)Cl).

Cross coupling with organotin reagents and comparison with Pd(phosphine) catalysts

Like in Pd-phosphine catalyzed reactions[2d], the Pd(Ar-BIAN) catalyzed cross coupling reactions using organotin reagents proceed with higher selectivity than the reactions with comparable organomagnesium and -zinc reagents (table 2). There is a high preference for cross coupling and in most cases no homocoupled products were detected by GC and NMR. Only in the reaction of benzyl bromide with tetramethyltin and benzoyl chloride with (2-furyl)trimethyltin some homocoupling occurred. In the absence of a Pd(Ar-BIAN) catalyst no reaction was observed.

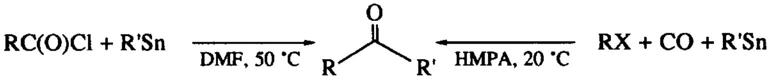
From the reaction of benzyl bromide with tetramethyltin it appeared that the coupling reactions proceed best when a Pd(Ar-BIAN)(dmfu) catalysts is used in polar aprotic solvents like N,N-dimethylformamide (DMF) at 50 °C or hexamethylphosphorous triamide (HMPA) at 20 °C. When employing 1 % of a $PdCl_2$(Ph-BIAN) catalyst in DMF at 50 °C, only 27 % conversion was achieved after 16 hours. Benzyl chloride reacted much slower with tetramethyltin than benzyl bromide and only 7 % conversion was achieved under conditions where the latter gave complete conversion.

Reactions of aromatic halides with tetramethyltin reagents proceed slowly. *p*-Iodotoluene gave only 41 % conversion with 1 % Pd(Ar-BIAN)(dmfu) catalyst after 18 hours (in DMF at 50 °C), whereas no conversion was observed in the reaction of bromobenzene with tetramethyltin. With *p*-nitrophenyl bromide there was some conversion to *p*-nitrotoluene in HMPA at 20 °C (10 % in 5 h). The rate of the reaction of iodobenzene with vinyltrimethyltin, catalyzed by Pd(*p*Tol-BIAN)(dmfu) is comparable to the $Pd(Ph_2PCH_2CH_2PPh_2)$ catalyzed reaction and is lower than the $Pd(PPh_3)_2$ catalyzed reaction[4b]. The reaction was not influenced by irradiation with a mercury lamp and addition of sodium bromide led to a slightly increased conversion (60 % vs 49 % in the absence of NaBr). When iodobenzene was reacted with a mixture of vinyltrimethyltin and tetramethyltin only styrene was formed and there was no evidence for any toluene, indicating that the transmetallation is 100 % selective.

Allylic halides react rapidly with phenyl- and *p*-tolyltin reagents in the presence of a Pd(Ar-BIAN) catalyst in DMF at 50 °C. Using 1 % Pd(*p*Tol-BIAN) catalyst, 2-methallyl chloride reacted within 40 minutes with phenyltributyltin to 2-methallylbenzene as the only product (turnover number ≥ 133 mol RX·(mol Pd)$^{-1}$·h^{-1}). By employing 1 % of a Pd(*p*Tol-DAB) catalyst, the reaction was also completed within 40 minutes, whereas only 8 % conversion was achieved in 62 minutes when 1 % of a $Pd(PPh_3)_2$ catalyst was used (turnover number = 7.7 mol RX·(mol Pd)$^{-1}$· h^{-1})[24]. The reaction of allyl bromide with *p*-tolyltin reagents to *p*-allyltoluene is slow at 20 °C in THF and HMPA and irradiation does not accelerate the reaction, but in DMF at 50 °C complete conversion is achieved within 16 hours (conditions are not optimized and reactions were carried out overnight to ensure complete conversion).

Pd(Ar-BIAN) catalyzed synthesis of ketones

The synthesis of ketones by using Pd(Ar-BIAN) catalysts, similar to the palladium-phosphine catalyzed Stille-type reactions[2d], is demonstrated by the coupling of acyl chlorides with organo-tin reagents and by the reaction of organic halides with organotin reagents under an atmosphere of carbon monoxide (equation 1). These reactions are highly selective, since in general the ketone was formed as the only product in good chemical yield (79-98 %).

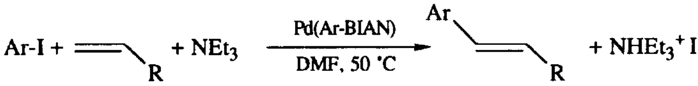


(1)

The rate of the PdL_2 catalyzed reaction of benzoyl chloride with (2-furyl)trimethyltin in refluxing THF decreased in the order L = PPh_3 >> dppe ≈ *p*Tol-BIAN. When a Pd(*p*Tol-BIAN) catalyst was used, initially fast conversion occurred, but after approximately 1 hour (40 % conversion) the reaction stopped almost completely. When an excess of *p*Tol-BIAN (2-5 eq. relative to Pd) was used the reaction was initially somewhat slower, but higher conversions were achieved (up to 75 %, comparable to the conversion of 80 % for the $Pd(Ph_2PCH_2CH_2PPh_2)$ catalyzed coupling). The $Pd(PPh_3)_2$ catalyzed reaction was not only faster in this case, but also proceeded with higher selectivity: only PhC(O)Fur was formed, whereas in the Pd(*p*Tol-BIAN) catalyzed reaction also some homocoupled products were formed (71 % PhC(O)Fur, 14 % Fur_2, 15 % $(PhC(O))_2$; Fur = 2-furyl).

Alkene insertion during the cross coupling reaction

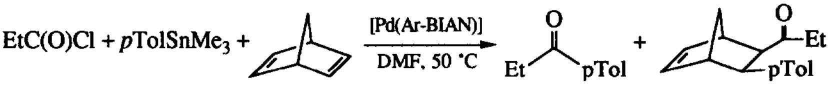
The possibility of alkene insertion after oxidative addition of an organic halide appears from the Pd(Ph-BIAN)(dmfu) catalyzed Heck-type reactions of iodobenzene or *p*-iodotoluene with styrene, methylacrylate and cyclopentene (equation 2), which proceed via alkene insertion followed by β-elimination[25].



(2)

In the Pd(Ar-BIAN) catalyzed cross coupling reaction no insertion of cyclopentene, styrene or methylacrylate in the coupling product was observed. Reaction of iodobenzene with sodium tetraphenylborate in the presence of cyclopentene showed no reaction, just as the reaction of *p*-iodotoluene with (*p*-tolyl)trimethyltin in the presence of methylacrylate. On the other hand the reactions of benzyl bromide or 2-methallyl chloride with (*p*-tolyl)tributyltin in the presence of styrene led only to the formation of the direct coupling products, at approximately the same rate as the reactions in the absence of styrene. When cross coupling reactions were carried out in the presence of the strained alkenes norbornadiene and norbornene, (partial) alkene insertion into the coupling product occurred, comparable to previously reported palladium-phosphine catalyzed reactions[26].

Facile, stoichiometric insertion of strained alkenes, such as norbornadiene, norbornene and dicyclopentadiene in palladium-carbon bonds has been reported[27]. Reaction of propionyl chloride with (*p*-tolyl)trimethyltin and norbornadiene gave apart from 55 % *p*TolC(O)Et also 45 % $EtC(O)C_7H_8pTol$ (equation 3). Reaction of iodobenzene with vinyltrimethyltin and norbornene led to the formation of $PhC_7H_{10}CH{=}CH_2$ and styrene (in a 2.3 : 1 ratio) and reaction of iodobenzene with phenyltrimethyltin and norbornene led to the formation of about 35 % $PhC_7H_{10}Ph$.



(3)

Stoichiometric reactions

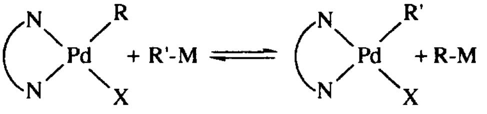
Stoichiometric reactions of organopalladium(Ar-BIAN) complexes, obtained by oxidative addition[28], with organotin reagents were studied by ^1H NMR in $CDCl_3$. No evidence for the formation of a diorganopalladium(Ar-BIAN) complex, via substitution of the halide by an organic group of the tin reagent, was obtained for any of the reactions studied. The only products that could be characterized were cross coupling products and uncoordinated Ar-BIAN. The reactions were slow in all cases and were accompanied by considerable decomposition: $Pd(C(O)Et)Cl(p\text{-}MeOC_6H_4\text{-}BIAN)$ + $pTolSnMe_3$ gave 23 % *p*TolC(O)Et after 7h and 53 % after 74 h; $Pd(Me)Cl(p\text{-}MeOC_6H_4\text{-}BIAN)$ and $PdBr(CH_2Ph)(p\text{-}MeOC_6H_4\text{-}BIAN)$ + $PhSnMe_3$ gave 21 % toluene and 25 % diphenylmethane after 24 hours, respectively.

DISCUSSION

Cross coupling with organomagnesium and -zinc reagents

The Pd(Ar-BIAN) catalyzed reaction of organic halides with organomagnesium and zinc reagents proceeds readily in THF at 20 °C. The rate determining step for these reactions might be oxidative adition of the organic halide, as has been shown for the Pd(Ar-BIAN) catalyzed coupling of benzyl bromide with *p*-tolyl magnesium and zinc reagents[23]. In most cases the reactions are accompanied by the formation of homocoupled products. The greater propensity of organozinc reagents to give cross coupling, as compared to organomagnesium reagents, has been observed before[29].

It has been shown in a detailed study[23] that in Pd(Ar-BIAN) catalyzed cross coupling reactions the formation of homocoupled products is due to exchange of the organic groups between palladium and magnesium or zinc (equation 4).



(M = Mg, Zn, Sn) (4)

The mixture of two organopalladium compexes and two transmetallating reagents can in principle combine in four different ways, leading to either cross or homocoupled product. The influence of the organic halide and the transmetallating reagent on the amount of homocoupled products formed can be explained by invoking[23] (i) the rate of exchange of organic groups between palladium and the transmetallating reagent, as compared to the rate of transmetallation and C-C bond formation and (ii) the relative rate of the reactions leading to homocoupling (RR and R'R') as compared to the reactions leading to cross coupling (RR').

The observation that the aromatic substituent of the Ar-BIAN ligand (Ar = Ph, *p*Tol, $p\text{-}MeOC_6H_4$) has no influence on the rate of the coupling reaction or the product distribution is consistent with the fact that these substituents impose comparable steric requirements in the vicinity of palladium and with the similar electronic properties of these Ar-BIAN ligands[16c,30].

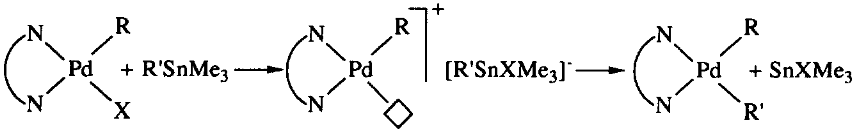
Cross coupling with organotin reagents and comparison with Pd(phosphine) catalysts

According to the generally accepted mechanism of palladium and nickel catalyzed cross coupling reactions (scheme 1), a sequence of oxidative addition, transmetallation and reductive elimination occurs. A separate study revealed that the oxidative addition of the organic halides employed in this work is faster than cross coupling under the experimental conditions of the coupling reaction[28]. Furthermore, in the reactions of the oxidative addition products with stoichiometric amounts of the organotin compounds, no intermediate diorganopalladium(Ar-BIAN) complex could be observed, only cross coupling products and free Ar-BIAN. These results indicate that transmetallation is the rate determining step in the Pd(Ar-BIAN) catalyzed coupling of organic halides with organotin reagents, which finding is in agreement with earlier studies on palladium-phosphine catalyzed reactions[2d,4b]. Furthermore, it is anticipated that transmetallation is slower for complexes with good σ-donor ligands, such as Ar-BIAN, as compared to phosphines[4b]. Oxidative addition becomes the rate determining step when organic halides are used that undergo less facile oxidative addition, such as benzyl chloride and bromobenzene[28] and in these cases no or only very low conversions were achieved.

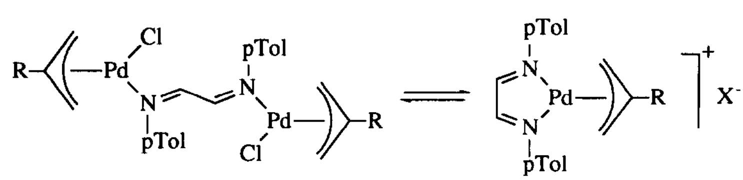
The necessity of polar aprotic solvents for the coupling reactions and the low conversions in less polar solvents indicates that transmetallation occurs via a polar mechanism, probably an electrophilic attack of the palladium on the tin-bound carbon atom[2d].

Alternatively, halide abstraction from palladium may occur, followed by transfer of the organic group from tin to palladium, which is facilitated by the formation of the anionic tin compound (scheme 2). Mechanisms via radical pathways or electron transfer to tin[31] are less likely in view of the insensitivity to irradiation and the observation that the reactions of benzyl bromide and 2-methallyl chloride with (*p*-tolyl)tributyltin were not influenced by the addition of styrene.

Scheme 2.



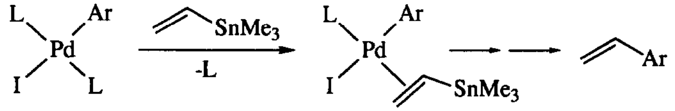
The coordination of the halide to tin prior to organic group transfer might explain the high rate of the Pd(Ar-BIAN) catalyzed reaction of allylic halides with organotin reagents, since a cationic $[Pd(\eta^3\text{-allyl})(Ar\text{-}BIAN)]$ X complex is involved which can easily transfer the halide to tin. When employing a Pd(*p*Tol-DAB) catalyst, also fast coupling of allylic halides with organotin reagents was observed, whereas it is known that oxidative addition of 2-methallyl chloride to Pd(*t*Bu-DAB)(dmfu) leads to a *t*Bu-DAB-bridged neutral complexes $[\{Pd(\eta^3\text{-allyl})Cl\}_2(\mu\text{-}t\mathrm{BuDAB})]$ and free *t*Bu-DAB[32]. Under the conditions of the catalytic coupling reactions probably this dinuclear complex is in fast equilibrium with cationic complexes containing a chelating *p*Tol-DAB ligand $[Pd(\eta^3\text{-allyl})(p\mathrm{Tol\text{-}DAB})]^+X^-$ (X = halide or $[Pd(\eta^3\text{-allyl})Cl_2]^-$)[33] (equation 5), which rapidly react with the organotin reagent in a subsequent step.



(5)

The fact that the $Pd(PPh_3)_2$ catalyzed reactions proceed much slower can be explained by the formation of a neutral $Pd(\eta^3\text{-allyl})X(PPh_3)$ complex and free PPh_3. In this case the reaction to $[Pd(\eta^3\text{-allyl})(PPh_3)_2]^+X^-$ will be much slower due to the different steric and electronic properties of PPh_3 as compared to *p*Tol-DAB.

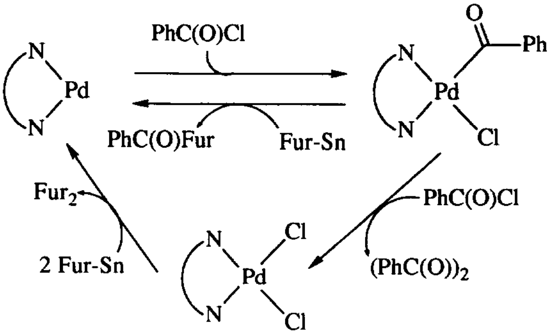
The reactions of iodobenzene with vinyltrimethyltin and benzoyl chloride with (2-furyl)trimethyltin are less efficiently catalyzed by Pd(Ar-BIAN) complexes, as compared to palladium-phosphine analogues. The palladium-phosphine catalyzed coupling of iodobenzene with vinyltrimethyltin proceeds via initial π-coordination of the vinyltin reagent to palladium with concomitant dissociation of a phosphine ligand (equation 6)[4b].



(6)

For chelating ligands, especially the rigid Ar-BIAN, dissociation of one of the chelating atoms is unlikely. In this case the reaction might in principle occur via dissociation of iodide from palladium and π-coordination of the tin reagent. However, the slightly increased rate observed upon addition of sodium bromide, disagrees with this mechanism and suggests that transmetallation preceded by coordination of the halide to tin is more likely (scheme 2).

The Pd(*p*Tol-BIAN) catalyzed reaction of benzoyl chloride with (2-furyl)trimethyltin in refluxing THF suffers from rapid catalyst deactivation. A likely explanation is the formation of $PdCl_2$(*p*Tol-BIAN) and $(PhC(O))_2$ by oxidative addition of benzoyl chloride to Pd(COPh)Cl(*p*Tol-BIAN) (scheme 3), comparable to the observed reaction of Pd(*p*Tol-BIAN)(dmfu) with excess acetyl chloride to give $PdCl_2$(*p*Tol-BIAN)[28]. The low catalytic activity of the $PdCl_2$(Ar-BIAN) complexes in cross coupling reactions with organotin reagents was also observed in other reactions (vide supra). This sequence of reactions can also explain the formation of homocoupled products in this specific case.



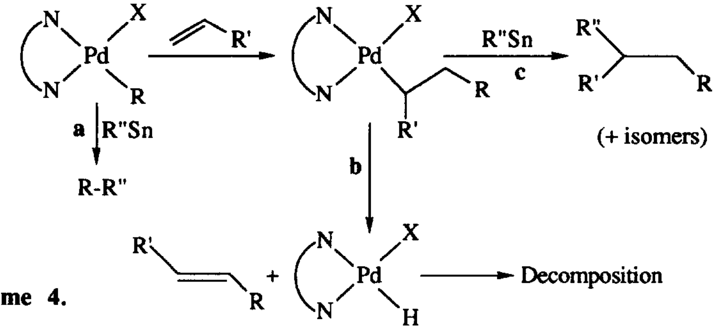
Scheme 3.

When phosphines are coordinated to palladium, catalyst deactivation occurs less readily because PhC(O)Cl reacts much slower with $Pd(C(O)Ph)Cl(PPh_3)_2$, due to the decreased nucleophilicity of palladium in this phosphine complex as compared to the Ar-BIAN analogue. Reactions of acyl halides with organotin reagents, which were performed in DMF at 50 °C, instead of in THF gave complete conversion without the formation of homocoupled products, indicating that under these conditions Pd(C(O)R)Cl(Ar-BIAN) reacts faster with the organotin compound than with the acyl halide, which is in agreement with a polar mechanism of transmetallation.

Insertion of carbon monoxide and alkenes during the cross coupling reaction

The high efficiency and selectivity of the carbonylative coupling can be explained by the high rate of insertion of carbon monoxide in palladium-carbon bonds of complexes containing Ar-BIAN ligands and the slow deinsertion of CO from acylpalladium(Ar-BIAN) complexes[27f].

Pd(Ar-BIAN) catalyzed Heck-type reactions showed that insertion of cyclopentene, styrene and methylacrylate in Pd-aryl σ-bonds is possible. The observation that no reaction occurred between aryl iodides and organotin reagents (or $NaBPh_4$) in the presence of these alkenes indicates that after oxidative addition alkene insertion occurs faster than transmetallation, followed by β-elimination and catalyst decomposition (scheme 4, route **b**). On the other hand, the formation of only direct coupling products in the reaction of benzyl bromide and 2-methallyl chloride with organotin reagents in the presence of styrene indicates that alkene insertion is slow relative to transmetallation in these cases (scheme 4, route **a**). The strained alkenes norbornadiene and norbornene can be (partially) inserted during cross coupling and similar products to those reported earlier[26] were obtained (scheme 4, route **c**).



Scheme 4.

CONCLUSION

Zerovalent Pd(Ar-BIAN)(dmfu) and divalent $PdCl_2$(Ar-BIAN) complexes (Ar = C_6H_5, *p*-MeC_6H_4, *p*-$MeOC_6H_4$) are good catalysts for carbon-carbon cross coupling reactions. When employing reactive transmetallating reagents such as organomagnesium and -zinc reagents, in general fast reactions are observed and the oxidative addition of the organic halide is probably rate determining, just as was observed in the Pd(*p*Tol-BIAN) catalyzed reaction of benzyl bromide with *p*-tolyl magnesium bromide[23]. By employing less reactive organotin reagents the coupling reaction is much slower and transmetallation becomes the rate determining step, but the selectivity for cross coupling is greater as compared to reactions employing organomagnesium and -zinc reagents.

It has been shown that in some cases the Pd(Ar-BIAN) catalysts give better results than their phosphine analogues (in terms of reaction rates and/or product yields). In other cases palladium-phosphine catalyzed reactions proceed more efficiently, due to faster reactions or slower catalyst deactivation. These observations support our idea that palladium catalysts with phosphines and (bidentate) nitrogen ligands complement each other and that the introduction of Pd(NN) catalysts widen the scope of palladium catalyzed reactions. This appeared also from the activity of Pd(Ar-BIAN)(alkene) complexes in catalytic homogeneous hydrogenation of electron poor alkenes[12], whereas comparable Pd-phosphine complexes were inactive. Our investigations on palladium catalyzed carbon-carbon bond forming reactions with this and other types of (bidentate) nitrogen ligands will continue in the future.

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