University of Groningen

Fast Palladium Catalyzed Arylation of Alkenes Using Bulky Monodentate Phosphorus Ligands

Strijdonck, Gino P.F. van; Boele, Maarten D.K.; Kamer, Paul C.J.; Vries, Johannes G. de; Leeuwen, Piet W.N.M. van

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
1999

[Link to publication in University of Groningen/UMCG research database](#)

Fast Palladium Catalyzed Arylation of Alkenes Using Bulky Monodentate Phosphorus Ligands

Gino P. F. van Strijdonck,[a] Maarten D. K. Boele,[a] Paul C. J. Kamer,[a] Johannes G. de Vries,*[b] and Piet W. N. M. van Leeuwen*[a]
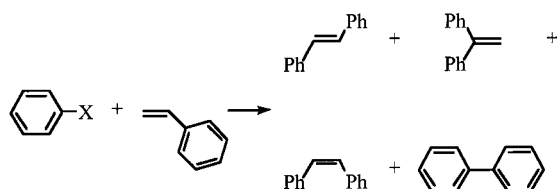
Complex **1b** shows an unprecedented high activity in the Heck reaction. Kinetic studies show that in this system not the oxidative addition but the alkene coordination/migratory insertion is the rate determining step.

The palladium-catalyzed arylation of alkenes, also known as the Heck reaction, has proven to be a versatile method for the formation of carbon−carbon bonds.[1] The Heck reaction is compatible with a broad range of substituents, but it also suffers from severe drawbacks which often preclude industrial use.[2] Even though some progress has been reported towards catalyst performance,[3] there is still a need for better catalysts.

Ligand effects[4] have been studied extensively for many metal catalyzed reactions. In the Heck reaction mainly phosphanes have been used. In a limited amount of papers the use of 1,10-phenanthroline derivatives has been reported[5] and recently phosphites were used.[6] Pfaltz and co-workers have reported on the use of mixed phosphane oxazoline ligands in an enantioselective Heck reaction.[7] Phosphorus amidites form a unique class of ligands, which have proven their usefulness in catalysis.[8] Their electronic properties are in between those of phosphanes and phosphites. As part of our studies on ligand effects, we decided to study the effect of phosphorus amidites and phosphites in the Heck reaction.

As a model reaction to study the effect of electronic and steric properties of the ligands on the Heck reaction we have chosen the reaction of iodobenzene with styrene in acetonitrile and triethylamine as a base.

The use of 1 mol-% of Pd(dba)$_2$ and 2 equivalents of phosphorus amidite **1b** (80°C) resulted in the very fast formation of mainly *trans*-stilbene, the Heck product (Scheme 1). In a series of ligands with approximately the same steric bulk the order of activity was found to be: phosphorus amidites (**1**) > phosphites (**3**) > phosphanes (**2**). Within a series of phosphorus amidite ligands with increasing steric bulk, ligand **1b** gave the fastest catalysis. In the phosphane and phosphite series a similar trend was observed, viz. **b** > **a** > **c** (see Table 1). When more equivalents of ligands are used, the activity drops, except for **1b**. Addition of more equivalents of this ligand does not affect the activity. Using the more bulky ligands **c**, relatively more of the *cis* product and less *trans*-stilbene was found with increasing L/Pd ratio.
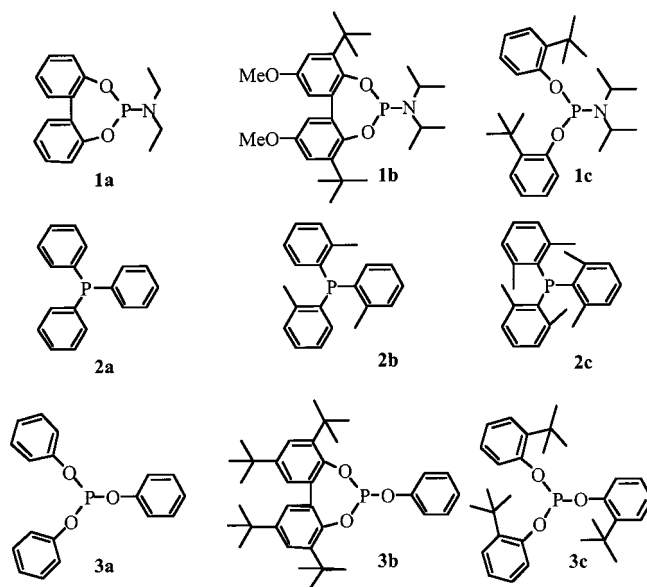
Figure 1. Monodentate ligands

Scheme 1. Heck reaction of styrene with phenyl halides

The use of Pd(dba)$_2$ without an additional ligand resulted in a low conversion and the formation of palladium black. The same was observed using Pd(OAc)$_2$ without additional ligand.

Recently, Beller and co-workers reported on cyclometallated palladium complexes as efficient catalysts for Heck

[a] Institute for Molecular Chemistry, Department of Inorganic Chemistry, University of Amsterdam,
Nieuwe Achtergracht 166, NL-1018 WV Amsterdam, The Netherlands
Fax: (internat.) +31-20/525-6456
E-mail: PWNM@anorg.chem.uva.nl
[b] DSM Research, Dept. Fine Chemicals,
P.O. Box 18, NL-6160 MD Geleen, The Netherlands

J. G. de Vries, P. W. N. M. van Leeuwen et al.
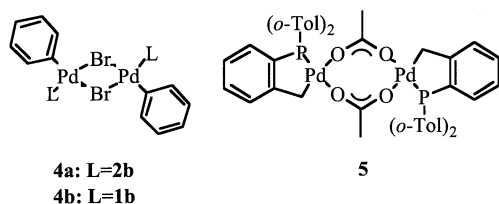
Figure 2. Pd^{II} compounds

reactions.[3d] Palladacycle **5**, however, was not very active in the reaction of iodobenzene with styrene in acetonitrile and triethylamine as a base. Probably the formation of the active species[3f] is slow under the conditions employed.

Table 1. Heck reaction of iodobenzene and styrene[a]

Catalyst	Conversion[b] [%]	Selectivity[c]		
		trans-stilbene [%]	*cis*-stilbene [%]	1,1-diphenyl-ethylene [%]
Pd(OAc)$_2$	5	90	1	9
Pd(dba)$_2$	7	90	1	9
Pd(dba)$_2$/**1a**	18	90	1	9
Pd(dba)$_2$/**1b**	100	90	1	9
Pd(dba)$_2$/**1c**	6	88	1	11
Pd(dba)$_2$/**2a**	6	90	1	9
Pd(dba)$_2$/**2b**	12	90	1	9
Pd(dba)$_2$/**2c**	1	89	1	10
Pd(dba)$_2$/**3a**	8	90	1	9
Pd(dba)$_2$/**3b**	48	90	1	9
Pd(dba)$_2$/**3c**	6	85	1	14
5	8	90	1	9

[a] Conditions: see Experimental Section. − [b] Based on iodobenzene, measured after 45 minutes. − [c] Less than 1% biphenyl was formed.

Phosphorus amidite **1b** gave the most active catalyst. To obtain further details of the catalytic cycle, we performed a kinetic study. To avoid interference of equilibria between the pre-catalyst and the intermediates involved in the catalytic cycle[9], we prepared compound **4b** and compared its catalytic behavior with that of tris(*o*-tolyl)phosphane-coordinated complex **4a** in the reaction of iodobenzene with styrene. Osmometric molecular mass determination in dichloromethane showed that compound **4b** exists as a dimer. A broad signal at δ = 118.3 in the ^{31}P-NMR spectrum is indicative of a fast equilibrium between the *cis* and the *trans* isomers[10]. After cooling the solution to 240 K we observed two sharp peaks at δ = 119.8 and 117.5 in a 4:3 ratio. The major product is probably the *trans* product. In acetonitrile, only one sharp singlet was observed at δ = 122.3 in a temperature range of 255−335 K.

The rate of the reaction between iodobenzene and styrene catalyzed by palladium complexes **4** was independent of the concentration of iodobenzene (0.10−2.0 M) and the concentration of triethylamine (0.16−2.5 M). Figure 3 shows a linear dependence of the initial turn over frequency (TOF$_{ini}$) on the styrene concentration (0−4.0 M). The reaction rate increases linearly with the square root of the palladium concentration (0−4.0 mM; see Figure 4). Using palladium concentrations below 4.0 mM and conversions up to 70% no formation of palladium black was observed.

The rate of the Heck reaction shows a large dependence on the solvent and the alkene used. In acetonitrile, the reaction of iodobenzene with styrene (1 M), catalyzed with 0.125 mol-% complex **4b** (0.25% Pd) gave 50% conversion after 2 h. In DMF, the conversion after 2 h. was 75%. In *N*-methyl pyrrolidinone (NMP) the reaction was even faster: within 45 minutes the reaction was completed. Reaction of iodobenzene with *n*-butylacrylate, in NMP at 80°C with 0.125 mol-% complex **4b**, was completed within 6 minutes. This reaction was more than 99% selective towards the *trans* coupled product. With this system we do not only have an extremely fast but also a stable catalyst and a very high turn-over number (> 500 000) has been obtained.
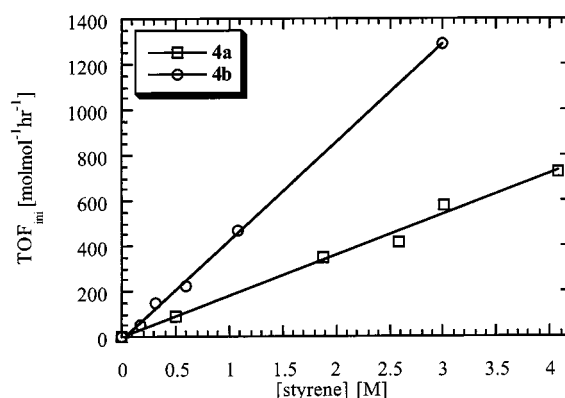
Figure 3. Plot of TOF$_{ini}$ versus [styrene] for the reaction of iodobenzene with styrene in CH$_3$CN at 65°C catalyzed with complexes **4** (TOF$_{ini}$ is the amount of products formed per mol Pd per hour after 5 min)
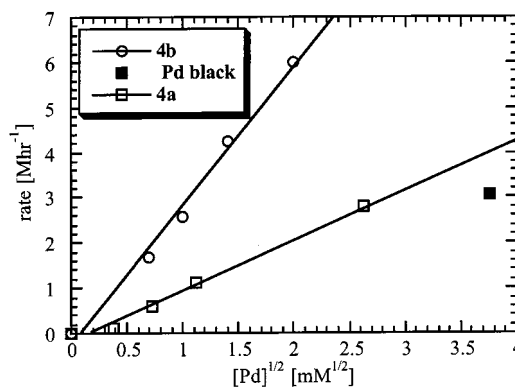
Figure 4. Plot of the rate versus [Pd]$^{1/2}$ for the reaction of iodobenzene with styrene in CH$_3$CN at 65°C catalyzed with complexes **4** (rate = *d*[products]/*d*t, measured after 5 min)

The unique kinetic observations are rationalized in terms of the catalytic cycle shown in Figure 5. In this cycle oxidative addition of an aryl halide to [PdL] gives a Pd^{II} compound which is in fast equilibrium with its dimer. The monomer forms a complex with the alkene. Next, the migratory insertion of this alkene takes place. After β-hydrogen elimination and reductive elimination of HX, the intermediate palladium(0) species with one ligand per palladium is obtained again.

Studies on phosphapalladacycles in the Heck reaction[3f,11] suggest that a monophosphane palladium(0) species, [R$_3$P−Pd], is a crucial intermediate of the cycle. This species is presumed to undergo fast oxidative addition of aryl halides followed by a dimerization giving the known compound **4a**.[10] Molecular weight determinations indicated that also complex **4b** exists as a dimer.

After alkene coordination and subsequent insertion of the alkene, the reaction is assumed to follow the widely accepted[12] pathway shown in Figure 5.

This proposed cycle is consistent with the kinetic data. Kinetic studies on the use of diphosphane ligands in the palladium catalyzed reaction of iodobenzene with styrene showed that the oxidative addition is one of the slower steps of the catalytic cycle. Since in the case of the bulky monodentate ligands the rate is independent of the concentration of iodobenzene the oxidative addition is not the turn over limiting step in these systems. This is quite surprising since phosphorus amidites render palladium less electron rich than phosphanes. The reaction rate is linearly dependent on the square root of the palladium concentration and first order in styrene concentration. This means that in this system either the alkene complexation or the migratory insertion must be the turn over limiting step. This step proceeds faster for complex **4b** than for complex **4a**.[13]
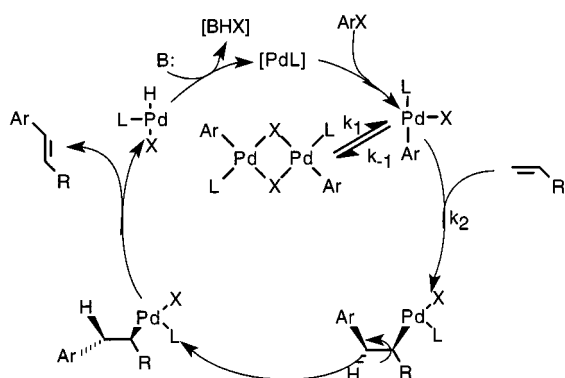

Figure 5. Postulated catalytic cycle for the Heck reaction; if we assume that $k_{-1} \gg k_1 \gg k_2$[alkene], then the rate = $k_2 K^{1/2}$[alkene][Pd]$^{1/2}$; $K = k_1/k_{-1}$

The subtle combination of electronic and steric properties of ligand **1b** results in a highly active catalyst for the Heck reaction. The ligand is sufficiently bulky to provide complexes having a Pd:P ratio of 1:1. A bulkier ligand, however, retards the reaction. The relatively small phosphorus amidite **1a** forms a palladium compound with two ligands under the reaction conditions as can be concluded from the NMR data.[14] This also decreases the activity of the catalyst.

In summary, the use of a bulky phosphorus amidite as ligand in the palladium-catalyzed arylation of alkenes resulted in an extremely active catalyst system. From kinetic studies we conclude that, under the reaction conditions employed, not the oxidative addition, but the coordination or insertion of the alkene is the rate-determining step in this reaction. Further exploration of the scope of the reaction

and the implications of the unprecedented kinetics are in progress.

Experimental Section

The ligands were prepared as described in the literature.[8a][15]

Complex **4a** was prepared as described by Hartwig.[11b] Complex **4b** was prepared in an analogous way in 81% yield. − C$_{68}$H$_{94}$Br$_2$N$_2$O$_4$Pd$_2$: calcd. C 54.38, H 6.31, N 1.86; found C 54.86, H 6.38, N 1.69. − ^{31}P{^{1}H} NMR (121 MHz, CDCl$_3$, 25°C, H$_3$PO$_4$): δ = 118.3 (s). − ^{1}H NMR (300 MHz, CDCl$_3$, 25°C, TMS): δ = 1.23 (s, 12 H, CH$_3$), 1.25 (s, 12 H, CH$_3$), 1.41 (s, 36 H, *t*Bu), 3.81 (s, 12 H, CH$_3$O), 4.45 (m, 4 H, CH), 6.62 (m, 10 H, ArH), 6.81 (m, 4 H, ArH), 6.94 (m, 4 H, ArH). − ^{13}C{^{1}H} NMR (78 MHz, CDCl$_3$, 25°C, TMS): δ = 25.0 (CH$_3$), 31.7 (*t*Bu), 35.6 (C), 49.9 [d, ^2J(C,P) = 18 Hz, CH], 50.0 (CH), 55.4 (CH$_3$O), 113.2 (ArH), 114.5 (ArH), 117.1 (Ar), 122.7 (ArH), 126.7 (ArH), 131.3 (Ar), 135.2 (ArH), 141.9 (Ar), 143.0 [d, ^2J(C,P) = 14 Hz, Ar], 155 (Ar).

Catalysis with in situ Prepared Catalysts: Under a dinitrogen atmosphere, a Schlenk vessel, fitted with a septum, was charged with Pd(dba)$_2$ (26.1 mg, 0.05 mmol) and ligand (0.1 mmol). Subsequently, 5 mL of freshly distilled acetonitrile (CaH$_2$), 250 µL of decane (1.28 mmol) as internal standard, 550 µL of iodobenzene (4.9 mmol) and 650 µL of styrene (5.5 mmol) were injected. The Schlenk vessel was heated to 80°C and 750 mL of triethylamine (5.4 mmol) was added. The reactions were monitored by gas chromatography (DB1 column).

Kinetic Studies: Under a dinitrogen atmosphere, a Schlenk vessel, fitted with a septum, was charged with complex **4**. Subsequently, freshly distilled acetonitrile (to a total volume of 10 mL), 500 µL of decane (2.56 mmol) as internal standard, iodobenzene, and styrene were injected. The Schlenk vessel was heated to 65°C and triethylamine was added (*t* = 0). The reactions were monitored by gas chromatography (DB1 column).

Catalysis with Complex 4a: Under a dinitrogen atmosphere, a Schlenk vessel, fitted with a septum, was charged with complex **4a** (9.4 mg, 0.00625 mmol). Subsequently, 5 mL of freshly distilled solvent, 250 µL of decane (1.28 mmol) as internal standard, 550 µL of iodobenzene (4.9 mmol) and alkene (5.5 mmol) were injected. The Schlenk vessel was heated to 80°C and 750 mL of triethylamine (5.4 mmol) was added. The reactions were monitored by gas chromatography (DB1 column).

[1] [1a] R. F. Heck, *Acc. Chem. Res.* **1979**, *12*, 146−151. − [1b] R. F. Heck, *Org. React.* **1982**, *27*, 345−390. − [1c] A. de Meijere, F. E. Meyer, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2379−2411; *Angew. Chem.* **1994**, *106*, 2473−2506. − [1d] W. Cabri, I. Candiani, *Acc. Chem. Res.* **1995**, *28*, 2−7. − [1e] T. Jeffery, *Tetrahedron* **1996**, *52*, 10113−10130.

[2] M. S. Stephan, A. J. M. Teunissen, G. K. M. Verzijl, J. G. de Vries, *Angew. Chem. Int. Ed.* **1998**, *37*, 662−663; *Angew. Chem.* **1998**, *110*, 668−690.

[3] [3a] Y. Ben-David, M. Portnoy, M. Gozin, D. Milstein, *Organometallics* **1992**, *11*, 1995−1996. − [3b] M. Portnoy, Y. Ben-David, D. Milstein, *Organometallics* **1993**, *12*, 4734−4735. − [3c] M. Portnoy, Y. Ben-David, I. Rousso, D. Milstein, *Organometallics* **1994**, *13*, 3465−3479. − [3d] W. A. Herrmann, C. Brossmer, K. Öfele, C.-P. Reisinger, T. H. Riermeier, M. Beller, H. Fischer, *Angew. Chem. Int. Ed.* **1995**, *34*, 1844−1847; *Angew. Chem.* **1995**, *107*, 1989−1992. − [3e] W. A. Herrmann, C. Brossmer, C.-P. Reisinger, T. H. Riermeier, K. Öfele, M. Beller, *Chem. Eur. J.* **1997**, *3*, 1357−1364. − [3f] M. Beller, T. H. Riermeier, *Eur. J. Inorg. Chem.* **1998**, 29−35. − [3g] M. Ohff, A. Ohff, M. van der Boom, D. Milstein, *J. Am. Chem. Soc.* **1997**,

119, 11687−1688. − [3h] M. R. Reetz, G. Lohmer, R. Schwickardi, *Angew. Chem. Int. Ed.* **1998**, *37*, 481−483; *Angew. Chem.* **1998**, *110*, 492−495.

[4] The Tolman parameters θ and χ are commonly used as a measure for the ligand parameters. C. A. Tolman, *Chem. Rev.* **1977**, *77*, 313−348.

[5] [5a] W. Cabri, I. Candiani, A. Bedeschi, R. Santi, *J. Org. Chem.* **1993**, *58*, 7421−77427. − [5b] K. H. Ang, S, Bräse, A. G. Steinig, F. E. Meyer, A. Lleboria, K. Voigt, A. de Meijere, *Tetrahedron* **1996**, *52*, 11503−11528. − [5c] D. Grotjahn, X. Zhang, *J. Mol. Catal. A: Chem.* **1997**, *116*, 99−107.

[6] [6a] M. Beller, A. Zapf, *Synlett.* **1998**, 792−793. − [6b] D. A Albisson, R. B. Bedford, S. E. Lawrence, P. N. Scully, *J. Chem. Soc.,Chem. Commun.* **1998**, 2095−2096.

[7] O. Loiseleur, M. Hayahashi, N. Schmees, A. Pfaltz, *Synthesis*, **1997**, 1338−1345.

[8] [8a] A. van Rooy, D. Burgers, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Recl. Trav. Chim. Pays-Bas* **1996**, *115*, 492−498. − [8b] A. H. M. de Vries, A. Meetsma, B. L. Feringa, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2374−2376; *Angew. Chem.* **1996**, *108*, 2526−2528. − [8c] B. L. Feringa, M. Pineski, L. A. Arnold, R. Imbor, A. H. M. de Vries, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2620−2623; *Angew. Chem.* **1997**, *109*, 2733−2736.

[9] It has been shown that dba retards the oxidative addition: C. Amatore, G. Broeker, A. Jutand, F. Khalil, *J. Am. Chem. Soc.* **1997**, *119*, 5176−5185.

[10] [10a] V. V. Grushin, H. Alper, *Organometallics* **1993**, *12*, 1890−1901. − [10b] F. Paul, J. Patt, J. F. Hartwig, *Organometallics* **1995**, *14*, 3037−3039.

[11] J. Louie, J. Hartwig, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2359−2361; *Angew. Chem.* **1996**, *108*, 2531−2533.

[12] [12a] Recently Shaw proposed an alternative mechanism involving Pd^{II}/Pd^{IV}: B. L. Shaw, *New. J. Chem.* **1998,** 77−79. − [12b] B. L. Shaw, S. D. Perera, E. A. Staley, *J. Chem. Soc., Chem. Commun.* **1998**, 1361−1362.

[13] When the more electron withdrawing phosphites are used it seems that the oxidative addition at palladium becomes rate limiting.

[14] Reaction of $Pd(dba)_2$ with various amounts of **2a** showed in the ^{31}P-NMR spectrum a singlet for the free ligand and two doublets [δ = 161.9 and δ = 163.9; $^2J(P,P) = 84$ Hz], assigned to $L_2Pd(dba)$.

[15] A. van Rooy, E. N. Orij, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Organometallics* **1995**, *14*, 34−43.