ELSEVIER

www.elsevier.nl/locate/jorganchem

Journal of Organometallic Chemistry 585 (1999) 348–352

Journal of Organometallic Chemistry

Priority Communication

Combining *N*-heterocyclic carbenes and phosphines: improved palladium(II) catalysts for aryl coupling reactions☆

Thomas Weskamp, Volker P.W. Böhm, Wolfgang A. Herrmann *

Anorganisch-chemisches Institut der Technischen Universität München, Lichtenbergstraße 4, D-85747 Garching bei München, Germany

Received 1 April 1999

Abstract

Complexes of the type (NHC)Pd(PR_3)I_2 with bulky *N*-heterocyclic carbenes (NHC) are efficient catalysts for aryl coupling reactions such as the Suzuki and Stille cross-coupling reaction. These catalysts combine the advantageous stability of bis(carbene) complexes and the good activity of the bis(phosphine) complexes in these reactions. Both arylbromides and arylchlorides can be used as substrates. © 1999 Elsevier Science S.A. All rights reserved.

Keywords: Catalysis; CC-Coupling; *N*-Heterocyclic carbenes; Phosphine; Palladium

1. Introduction

There has been a long-standing interest in the properties of palladium complexes because they are widely used as catalysts for carbon–carbon bond forming reactions [1]. These reactions are key steps in many syntheses of organic chemicals, natural products, as well as in a variety of industrial processes. Important examples for this type of catalysis are the Suzuki [2] and the Stille [3] cross-coupling reactions. The reason for the success of these reactions is the fact that they are known to work reliably and to tolerate most functional groups both on the substrates and the products.

Palladium(II) complexes of *N*-heterocyclic carbenes (NHC) are well known, and various routes to obtain them have been published [4,5]. One of their interesting characteristics is the extraordinary thermal stability and the high dissociation energies of the Pd–NHC bond [6]. These complexes have been successfully applied to Heck-type CC-coupling reactions [6,7] as well as ethylene/CO co-polymerisation [8]. Other metals have also shown catalytic activities with this type of ligand for a variety of different reactions [4b].

Phosphine complexes of palladium(II) are even better known and easily prepared from palladium(II) salts and an excess of phosphine ligand [9]. With these complexes the catalytic activity of palladium in various reactions including CC-coupling has been established for the first time [1]. Despite their activity as potential catalysts these complexes suffer from the fact that easy ligand dissociation leads to early palladium black precipitation as an unwanted side reaction [10]. The suppression of this side reaction combined with a retention of high activity in catalysis has ever since attracted much effort in the literature [11].

In olefin metathesis, mixed NHC–phosphine complexes of ruthenium proved to be more effective than the bis(carbene) or bis(phosphine) complexes [12]. This prompted us to test NHC–phosphine complexes of palladium for Heck-type reactions. In this paper we describe our preliminary results in the Suzuki and Stille cross-coupling reaction.

2. Results and discussion

The *trans*-NHC–phosphine complexes **2** are prepared from di(μ-iodo)-bis(1,3-di(1′-(*R*)-phenylethyl)imidazo-

☆ *N*-Heterocyclic Carbenes, part 21. Preceding paper in this series: W.A. Herrmann, M.G. Gardiner, J. Schwarz, M. Spiegler, J. Organomet. Chem. 575 (1999) 80–86.

* Corresponding author. Tel.: +49-89-2893080; fax: +49-89-28913473.

E-mail address: lit@arthur.anorg.chemie.tu-muenchen.de (W.A. Herrmann)

0022-328X/99/$ - see front matter © 1999 Elsevier Science S.A. All rights reserved.
PII: S0022-328X(99)00237-5

lin-2-ylidene)dipalladium(II) **1** by addition of the appropriate phosphine (Scheme 1). NMR experiments of complexes **2** show only one set of signals in a symmetrical surrounding indicating the exclusive formation of the *trans*-isomer. This observation can be readily explained by considering the sterical bulk of the 1,3-di(1′-(*R*)-phenylethyl)imidazolin-2-ylidene.

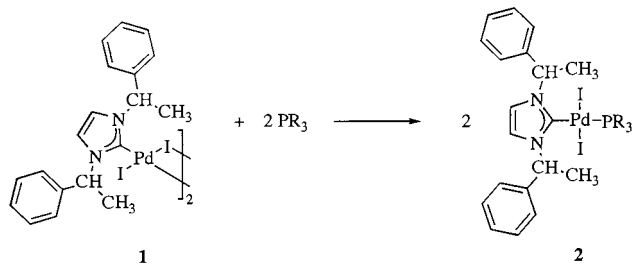
Palladium-catalyzed Suzuki and Stille cross-coupling reactions have both emerged powerful methods for the synthesis of unsymmetrical biaryls [2,3,13], which represent important structural units in drug intermediates [14] and in non-linear optical materials [15].

The new complexes **2** were tested in the Suzuki cross coupling of aryl halides and organoboronates using phenylboronic acid as the standard substrate and different aryl halides as the coupling partners (see Table 1). With bis(carbene) complexes of palladium(II) the use of potassium carbonate in toluene at 120°C results in optimized yields [7c]. Thus, similar conditions were applied to the mixed NHC–phosphine complexes: 1.0 equivalent aryl halide, 1.2 equivalents phenylboronic acid and 1.5 equivalents K_2CO_3 in xylene at 130°C work well both with bromoarenes and chloroarenes. Changing the base to potassium phosphate results in similar yields, but also produces early precipitation of palladium black. Sodium acetate or sodium fluoride do not give satisfactory results. Only the use of Cs_2CO_3 does result in higher yields, especially in the case of non-activated chloroarenes (Entries 8 and 9). Our preliminary results show that turnover numbers of up to 1000 [mol product/mol palladium] can be achieved with *p*-bromoacetophenone (Entry 2). Comparison with bis(1,3-dimethylimidazolin-2-ylidene)dipalladium(II) diiodide stresses the need for one phosphine ligand for the complex to be an active catalyst: the bis(carbene) complex does not show any catalytic activity with *p*-chloroanisole in this reaction under the conditions described above (Entry 11). The corresponding bis(phosphine) complexes $(R_3P)_2PdX_2$ are known to readily decompose to palladium black at elevated reaction temperatures whereas the stability of the NHC–phosphine complexes **2** is comparable to the one of the bis(carbene) complexes, i.e. palladium black precipitation only occurs after prolonged reaction times. Variation of the phosphine in the catalysts **2** exhibits only little effect with bromoarenes but results in dramatic changes in yield with chloroarenes. In the latter cases, only the basic tricyclohexylphosphine PCy_3 achieved high turnover numbers (Entries 7 and 8). Thus, with bromoarenes the economical triphenylphosphine PPh_3 is good enough whereas with chloroarenes the more expensive PCy_3 is to be used.

The Stille cross coupling of aryl halides and organostannanes was tested using tributylphenyltin as the standard substrate. Coupling with different aryl halides was achieved with the best conditions being 1.0 equivalent aryl halide and 1.2 equivalents tributylphenyltin in toluene or xylene at 110°C (see Table 2). The preliminary results show that turnovers are moderate to good with bromoarenes. At the same time the stability of the complexes **2** is excellent during catalysis, i.e. no palladium black precipitation occurs. This is not observed to be the case with the corresponding bis(phosphine) complexes under the same reaction conditions. The variation of the phosphine in compounds **2** shows the need for less basic triarylphosphines like PPh_3 as PCy_3 performs significantly worse (Entries 13 and 14). Dissociative ligands such as tris(2-furyl)phosphine $P(Fur)_3$ and triphenylarsine $AsPh_3$ can result in largely improved rates and yields [16] but this was not observed in our case although $P(Fur)_3$ was the second best phosphine we tested (Entries 15 and 16). Thus, we used PPh_3 as the standard ligand because of its economical advantage. The addition of Cu(I) salts does not show any promoting effect on the turnover numbers with our system although these salts have shown to be beneficial in other cases [17]. The transformation of chloroarenes is not possible under the described conditions (Entry 21).

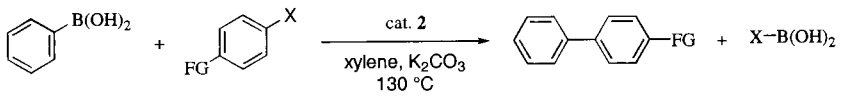
3. Conclusions

Using mixed NHC–phosphine complexes of palladium(II) for CC-coupling reactions is an excellent means of triggering both activity and stability of the catalytically active species. Our experiments demonstrate the applicability of these catalysts in Suzuki and Stille biaryl formation reactions with boronic acids and tributylstannanes. An important feature of the pre-catalysts is the necessity for bulky *N*-heterocyclic carbene ligands, whereas the phosphine ligand can be varied from triaryl- to trialkyl phosphines depending on the reaction and the substrate. To our knowledge, this is one of the most effective palladium(II) catalyst systems for these reactions and it is the first time that palladium complexes of *N*-heterocyclic carbenes have been reported to catalyze the Stille reaction. Only palladium(0) catalyst systems have shown significantly higher activities in the Suzuki reaction but have not been able to



Scheme 1. Preparation of *trans*-(1,3-di(1′-(*R*)-phenylethyl)imidazolin-2-ylidene)(phosphine)palladium(II) diiodide **2**, see Section 4.

Table 1
Suzuki cross-coupling reaction, FG = functional group [a]



Entry	X	FG	mol% Pd	Time (h)	PR_3 [b]	Yield (%) [c]
1	Br	$C(O)CH_3$	1.0	14	–	>99%
2	Br	$C(O)CH_3$	0.1	13	PPh_3	>99%
3	Br	H	1.0	13	PPh_3	>99%
4	Br	OCH_3	1.0	14	PPh_3	>99%
5	Br	OCH_3	1.0	12	PCy_3	>99%
6	Cl	$C(O)CH_3$	1.0	13	PCy_3	90%
7	Cl	H	1.0	13	PPh_3	7% [d]
8	Cl	H	1.0	13	PCy_3	42%
9	Cl	H	1.0	32	PCy_3	87%[d]
10	Cl	OCH_3	1.0	32	PCy_3	69%[d]
11	Cl	OCH_3	3.0 [e]		–	0%

[a] Reaction conditions: 1.0 equivalent ArX, 1.2 equivalents $PhB(OH)_2$, 1.5 equivalents base; for further conditions see Section 4.
[b] Cy = cyclohexyl, Ph = phenyl.
[c] GC-yield using diethyleneglycol-di-*n*-butylether as internal standard.
[d] Using Cs_2CO_3 as the base.
[e] Using bis(1,3-dimethylimidazolin-2-ylidene)palladium(II) diiodide as catalyst.

achieve comparable stabilities [11b,11c]. Therefore, we are currently investigating mixed NHC–phosphine complexes of palladium(0) as catalysts for Heck-type coupling reactions.

4. Experimental

Except for work-up of reactions, all operations were carried out under nitrogen. Xylene was degassed prior to use. Dichloromethane and toluene were dried and degassed according to a published procedure by Grubbs et al. [18]. NMP and DMF were degassed with nitrogen and dried over 4 Å molecular sieves.

1,3-Di(1′-(*R*)-phenylethyl)imidazolium chloride [19] and di(μ-iodo)-bis(1,3-di(1′-(*R*)-phenylethyl)imidazolin-2-ylidene)dipalladium(II) [7b] were prepared according to literature procedures.

4.1. Catalyst preparation

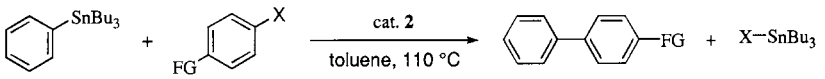
General procedure for the preparation of *trans*-(1,3-di(1′-(*R*)-phenylethyl)imidazolin-2-ylidene)(phosphine) palladium(II) diiodide **2**.

One equivalent di(μ-iodo)-bis(1,3-di(1′-(*R*)-phenylethyl)imidazolin-2-ylidene)dipalladium(II) is dissolved in 1 ml of the solvent used for catalysis. To the red solution one equivalent phosphine is added. The yellow mixture is stirred at room temperature for 10 min until being used for catalysis. The analytically pure compound can be obtained from CH_2Cl_2 by crystallisation, e.g. *trans*-(1,3-di(1′-(*R*)-phenylethyl)imidazolin-2-ylidene)(triphenylphosphine)palladium(II) diiodide. ^{1}H-NMR (400 MHz, CD_2Cl_2): $\delta = 1.93$ (6H, d, CH_3, $^3J(HH) = 7.3$ Hz); 6.34 (2H, q, NCH(Me)Ph, $^3J(HH) = 7.3$ Hz); 7.08 (2H, d, =CH, $^3J(PH) = 1.5$ Hz); 7.76–7.35 (25H, m, H_{Ph},); ^{13}C{^{1}H}-NMR (100.5 MHz, CD_2Cl_2): $\delta = 20.4$ (CH_3); 59.2 (NCH(Me)Ph); 120.0 (=CH, $^4J(PC) = 6.1$ Hz); 128.1 (Ph, $J(PC) = 10.0$ Hz); 128.3 (Ph); 128.4 (Ph); 128.8 (Ph); 130.5 (Ph, $^4J(PC) = 2.3$ Hz); 133.1 (Ph, $^1J(PC) = 44.6$ Hz); 135.6 (Ph, $J(PC) = 10.0$ Hz); 140.2 (Ph); 155.9 (C–Pd); ^{31}P{^{1}H}-NMR (161.9 MHz, CD_2Cl_2): $\delta = 16.5$; $C_{37}H_{35}I_2N_2PPd$ (898.90): Anal. Calc. C 49.44, H 3.92, N 3.12; Found C 49.55, H 3.69, N 3.32.

4.2. Suzuki reaction

A total of 1.2 equivalents of phenylboronic acid (146 mg, 1.2 mmol) and 1.5 equivalents of potassium carbonate (207 mg, 1.5 mmol) are placed in a Schlenk tube equipped with a stirring bar. The vessel is put under a nitrogen atmosphere and 1.0 equivalent of aryl halide (1.0 mmol; e.g. 187 mg bromoanisole, 125 μl), 0.1 mg diethyleneglycol-di-*n*-butylether and 2 ml of degassed xylene are added. After thermostating at 130°C for 10 min, the cataalyst solution (vide supra) is added against a positive stream of nitrogen. To finish the reaction, the mixture is allowed to cool to room temperature and 3 ml of water are added. The water phase is extracted three times with 2 ml of diethylether and the organic phases are dried with $MgSO_4$.

Table 2
Stille cross-coupling reaction, FG = functional group [a]



Entry	X	FG	mol% Pd	Time (h)	PR_3 [b]	Yield (%) [c]
12	Br	$C(O)CH_3$	1.0	17	–	11%
13	Br	$C(O)CH_3$	1.0	17	PPh_3	>99%
14	Br	$C(O)CH_3$	1.0	17	PCy_3	9%
15	Br	$C(O)CH_3$	1.0	17	$AsPh_3$	20%
16	Br	$C(O)CH_3$	1.0	17	$P(Fur)_3$	68%
17	Br	H	1.0	17	PPh_3	91%
18	Br	OCH_3	1.0	25	PPh_3	82%
19	Br	OCH_3	1.0	25	PCy_3	0%
20	Br	OCH_3	1.0	25	$P(Fur)_3$	33%
21	Cl	$C(O)CH_3$	1.0	17	PPh_3	4%

[a] Reaction conditions: 1.0 equivalent ArX, 1.2 equivalents $PhSnBu_3$; for further conditions see Section 4.
[b] Cy = cyclohexyl, Fur = 2-furyl, Ph = phenyl.
[c] GC-yield using diethyleneglycol-di-*n*-butylether as internal standard.

4.3. Stille reaction

A Schlenk tube equipped with a stirring bar is put under an atmosphere of nitrogen. 1.2 equivalents of tributylphenyltin (441 mg, 392 μl, 1.2 mmol), 1.0 equivalent of aryl halide (1.0 mmol; e.g. 187 mg bromoanisole, 125 μl), 0.1 mg diethyleneglycol-di-*n*-butylether and 2 ml of degassed and dry toluene are added. After thermostating at 110°C for 10 min the catalyst solution (vide supra) is added against a positive stream of nitrogen. To finish the reaction, the mixture is allowed to cool to room temperature and 3 ml of water are added. The water phase is extracted three times with 2 ml of diethylether and the organic phases are dried with $MgSO_4$.

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft (DFG), the Bayerischer Forschungsverbund Katalyse (FORKAT), Degussa AG (Pd salt grants) and the Fonds der Chemischen Industrie (studentships for V.P.W.B. and T. W.).

References

[1] J. Tsuji, Palladium Reagents and Catalysts, Wiley, Chichester, 1995.
[2] (a) N. Miyaura, A. Suzuki, Chem. Rev. 95 (1995) 2457. (b) A.R. Martin, Y.H. Yang, Acta Chem. Scand. 47 (1993) 221. (c) A. Suzuki, Pure Appl. Chem. 63 (1991) 419.
[3] (a) V. Farina, V. Krishnamurthy, W.J. Scott, Org. React. 50 (1997) 1. (b) T.N. Mitchell, Synthesis (1992) 803. (c) J.K. Stille, Angew. Chem. 98 (1986) 504; Angew. Chem. Int. Ed. Engl. 25 (1986) 508.
[4] (a) M. Regitz, Angew. Chem. 108 (1996) 791; Angew. Chem. Int. Ed. Engl. 35 (1996) 725. (b) W.A. Herrmann, C. Köcher, Angew. Chem. 109 (1997) 2256; Angew. Chem. Int. Ed. Engl. 36 (1997) 2162.
[5] (a) W.A. Herrmann, M. Elison, J. Fischer, C. Köcher, Chem. Eur. J. 2 (1996) 772. (b) M.J. Green, K.J. Cavell, B.W. Skelton, A.H. White, J. Organomet. Chem 554 (1998) 175. (c) W.A. Herrmann, J. Schwarz, M.G. Gardiner, M. Spiegler, J. Organomet. Chem. 575 (1999) 80.
[6] M.G. Gardiner, V.P.W. Böhm, J. Schwarz, W. Hieringer, W.A. Herrmann, Chem. Eur. J., submitted for publication.
[7] (a) W.A. Herrmann, M. Elison, J. Fischer, C. Köcher, G.R.J. Artus, Angew. Chem. 107 (1995) 2602; Angew. Chem. Int. Ed. Engl. 34 (1995) 2371. (b) D. Enders, H. Gielen, G. Raabe, J. Runsink, J.H. Teles, Chem. Ber. (1996) 1483. (c) W.A. Herrmann, C.-P. Reisinger, M. Spiegler, J. Organomet. Chem. 557 (1998) 93. (d) D.S. McGuinness, M.J. Green, K.J. Cavell, B.W. Skelton, A.H. White, J. Organomet. Chem. 565 (1998) 165.
[8] M.G. Gardiner, W.A. Herrmann, C.-P. Reisinger, J. Schwarz, M. Spiegler, J. Organomet. Chem. 572 (1999) 239.
[9] F. Ozawa, in: S. Komiya (Ed.), Synthesis of Organometallic Compounds, Wiley, Sussex, 1997, p. 249.
[10] W.A. Herrmann, in: B. Cornils, W.A. Herrmann (Eds.), Applied Homogeneous Catalysis with Organometallic Compounds, VCH, Weinheim, 1996, p. 712.
[11] see, e.g.: (a) M. Beller, H. Fischer, W.A. Herrmann, K. Öfele, C. Broßmer, Angew. Chem. 107 (1995) 1992; Angew. Chem. Int. Ed. Engl. 34 (1995) 1848. (b) A.F. Littke, G.C. Fu, Angew. Chem. 110 (1998) 3586; Angew. Chem. Int. Ed. 37 (1998) 3387. (c) D.W. Old, J.P. Wolfe, S.L. Buchwald, J. Am. Chem. Soc. 120 (1998) 9722.
[12] (a) T. Weskamp, F.J. Kohl, W. Hieringer, D. Glich, W.A. Herrmann, Angew. Chem. in press. (b) T. Weskamp, F.J. Kohl, W.A. Herrmann, J. Organomet. Chem., in press. (c) J. Huang,

E.D. Stevens, S.P. Nolan, J.L. Petersen, J. Am. Chem. Soc. 121 (1999) 2674. (d) M. Scholl, T.M. Trnka, J.P. Morgan, R.H. Grubbs, Tetrahedron Lett. 40 (1999) 2247. (e) L. Ackermann, A. Fürstner, T. Weskamp, F.J. Kohl, W.A. Herrmann, Tetrahedron Lett. in press. (f) U. Frenzel, T. Weskamp, F.J. Kohl, O. Nuyken, W.A. Herrmann, J. Organomet. Chem. in press. (g) T. Weskamp, W.C. Schattenmann, M. Spiegler, W.A. Herrmann, Angew. Chem. 110 (1998) 2631; Angew. Chem. Int. Ed. 37 (1998) 2490.

[13] S.P. Stanforth, Tetrahedron 54 (1998) 263.

[14] (a) K.-H. Hsieh, T. LaHann, R. Speth, J. Med. Chem. 32 (1989) 898. (b) D. Williams, R. Kannan, J. Org. Chem. 52 (1987) 5435.

[15] D.J. Williams, Angew. Chem. 96 (1984) 637; Angew. Chem. Int. Ed. Engl. 23 (1984) 640.

[16] (a) V. Farina, B. Krishnan, J. Am. Chem. Soc. 113 (1991) 9585. (b) A.M. Echavarren, N. Tamayo, D.J. Cárdenas, J. Org. Chem. 59 (1994) 6075.

[17] (a) F. Paul, J. Patt, J.F. Hartwig, Organometallics 14 (1995) 3030. (b) K.C. Nicolaou, M. Sato, N.D. Miller, J.L. Gunzner, J. Renand, E. Untersteller, Angew. Chem. 108 (1996) 952; Angew. Chem. Int. Ed. Engl. 35 (1996) 889. (c) M. Suzuki, H. Doi, M. Björkman, Y. Andersson, B. Langström, Y. Watanabe, R. Noyori, Chem. Eur. J. 3 (1997) 2039.

[18] A.B. Pangborn, M.A. Giardello, R.H. Grubbs, R.K. Rosen, F.J. Timmers, Organometallics 15 (1996) 1518.

[19] W.A. Herrmann, C. Köcher, L.J. Gooßen, G.R.J. Artus, Chem. Eur. J. 2 (1996) 1627.