ORGANIC LETTERS

2002
Vol. 4, No. 18
3031−3033

New Palladium Carbene Catalysts for the Heck Reaction of Aryl Chlorides in Ionic Liquids

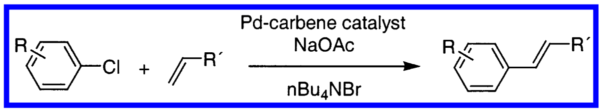
Kumaravel Selvakumar, Alexander Zapf, and Matthias Beller*

Institut für Organische Katalyseforschung an der Universität Rostock e. V. (IfOK), Buchbinderstrasse 5−6, D-18055 Rostock, Germany

matthias.beller@ifok.uni-rostock.de

Received May 21, 2002

ABSTRACT



The Heck reaction of aryl chlorides was investigated in the presence of defined monocarbenepalladium(0) complexes. Activated and nonactivated aryl chlorides provide the corresponding cinnamic esters and stilbenes in $^{n}Bu_4NBr$ as a ionic liquid in good to excellent yields.

Palladium-catalyzed coupling reactions of aryl chlorides are of general interest for the synthesis of organic building blocks and pharmaceutical and agrochemical derivatives. In addition to small-scale applications (from <1 to 100 g), there is an increasing awareness of this type of reaction for industrial fine chemical synthesis (from 1 to >100 t/a).[1] Regarding the availability and the economic viability, aryl chlorides are the most attractive starting materials among the different aryl halides. To develop palladium-catalyzed coupling reactions of aryl chlorides to a practical level, we started, some time ago, a research program on this topic. The palladacycles introduced by Herrmann and co-workers and us are stable and robust palladium catalysts for Heck and Suzuki coupling reactions of activated aryl chlorides with high turnover numbers.[2] However, the catalyst activity is not sufficient to allow an efficient activation of neutral and electron-rich aryl chlorides. Hence, we and other research groups[3] developed more active palladium catalysts based on sterically hindered basic phosphine ligands for aryl chloride activation. In this respect, we were the first to introduce diadamantylalkylphosphines as ligands for various coupling reactions with aryl chlorides.[4] In addition, we also demonstrated that basic chelating phosphines based on the ferrocene core allow carbonylation reactions of nonactivated chloroarenes.[5]

---

(1) (a) Beller, M.; Zapf, A.; Mägerlein, W. *Chem. Eng. Techn.* **2001**, *4*, 575. (b) Beller, M.; Zapf, A. *Top. Catal.* **2002**, *19*, 101. (c) de Vries, J. G. *Can. J. Chem.* **2001**, *79*, 1086.

(2) (a) Herrmann, W. A.; Brossmer, C.; Öfele, K.; Priermeier, T.; Beller, M.; Fischer, H. *Angew. Chem.* **1995**, *107*, 1989; *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1844. (b) Beller, M.; Fischer, H.; Herrmann, W. A.; Brossmer, C. *Angew. Chem.* **1995**, *107*, 1992; *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1848. (c) Beller, M.; Riermeier, T. H.; Haber, S.; Kleiner, H.-J.; Herrmann, W. A. *Chem. Ber.* **1996**, *129*, 1259. (d) Herrmann, W. A.; Brossmer, C.; Reisinger, C.-P.; Öfele, K.; Beller, M.; Riermeier, T. H. *Chem. Eur. J.* **1997**, *3*, 1357. (e) Beller, M.; Riermeier, T. H. *Eur. J. Inorg. Chem.* **1998**, 29. (f) Beller, M.; Riermeier, T. H.; Mägerlein, W.; Müller, T. E.; Scherer, W. *Polyhedron* **1998**, *17*, 1165. (g) Zapf, A.; Beller, M. *Chem. Eur. J.* **2001**, *7*, 2908.

(3) (a) Hillier, A. C.; Nolan, S. N. *Platinum Metals Rev.* **2002**, *46*, 50 and references therein. (b) Shaughnessy, K. H.; Kim, P.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 2123. (c) Hartwig, J. F.; Kawatsura, M.; Hauck, S. I.; Shaughnessy, K. H.; Alcazar-Roman, L. M. *J. Org. Chem.* **1999**, *64*, 5575. (d) Lee, S.; Hartwig, J. F. *J. Org. Chem.* **2001**, *66*, 3402. (e) Stambuli, J. P.; Stauffer, S. R.; Shaughnessy, K. H.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 2677. (f) Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 2719. (g) Klapars, A.; Antilla, J. C.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 7727. (h) Parrish, C. A.; Buchwald, S. L. *J. Org. Chem.* **2001**, *66*, 3820. (i) Grasa, G. A.; Viciu, M. S.; Huang, J.; Nolan, S. P. *J. Org. Chem.* **2001**, *66*, 7729. (j) Gstöttmayr, C. W. K.; Böhm, V. P. W.; Herdtweck, E.; Grosche, M.; Herrmann, W. A. *Angew. Chem.* **2002**, *114*, 1421; *Angew. Chem., Int. Ed.* **2002**, *41*, 1363. (k) Yin, J.; Rainka, M. P.; Zhang, X.-X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1162. (l) Beare, N. A.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 541.

(4) (a) Gómez Andreu, M.; Zapf, A.; Beller, M. *Chem. Commun.* **2000**, 2475. (b) Zapf, A.; Ehrentraut, A.; Beller, M. *Angew. Chem.* **2000**, *112*, 4315; *Angew. Chem., Int. Ed.* **2000**, *39*, 4153. (c) Ehrentraut, A.; Zapf, A.; Beller, M. *Synlett* **2000**, 1589. (d) Ehrentraut, A.; Zapf, A.; Beller, M. *J. Mol. Cat.* **2002**, *182−183*, 515. (e) Ehrentraut, A.; Zapf, A.; Beller, M. *Adv. Synth. Cat.* **2002**, *344*, 209.

(5) (a) Mägerlein, W.; Indolese, A.; Beller, M. *Angew. Chem.* **2001**, *113*, 2940; *Angew. Chem., Int. Ed.* **2001**, *40*, 2856. (b) Beller, M.; Mägerlein, W.; Indolese, A. F.; Fischer, C. *Synthesis* **2001**, 1098. (c) Beller, M.; Indolese, A. F. *Chimia* **2001**, *55*, 684. (d) Mägerlein, W.; Indolese, A. F.; Beller, M. *J. Organomet. Chem.* **2002**, *641*, 30.

10.1021/ol020103h CCC: $22.00

Scheme 1. Pd-Catalyzed Heck Reaction of Aryl Chlorides with Styrene

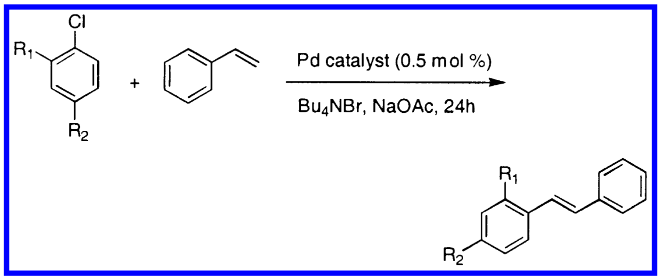
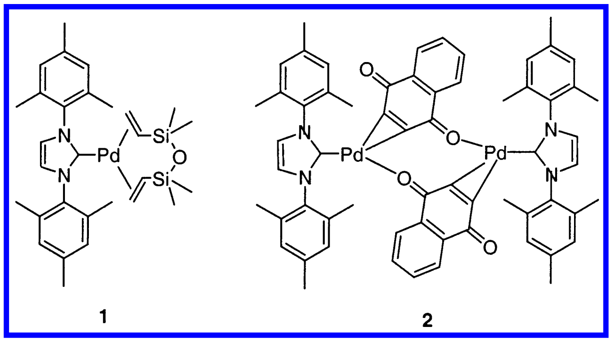


Table 1. Pd-Catalyzed Heck Reaction of Aryl Chlorides

entry	R^1	R^2	Pd catalyst	temp (°C)	conversion (%)	yield (%)
1	H	H	**1**	140	23	14
2	H	H	**2**	140	69	62
3	H	H	**3**	140	71	62
4	H	H	**2**	160	80	72
5	H	H	**3**	160	83	67
6	H	NO_2	**2**	140	100	92
7	H	NO_2	**3**	140	100	88
8	H	$COCH_3$	**2**	140	100	96
9	H	$COCH_3$	**3**	140	100	97
10	H	CF_3	**2**	140	88	86
11	H	CF_3	**3**	140	93	84
12	CN	H	**2**	140	100	94
13	CN	H	**3**	140	100	99
14	H	Me	**3**	140	40	39
15	H	Me	**3**	160	65	62

Recently, we became interested in the use of carbene ligands for palladium-catalyzed reactions. In the past few years, palladium carbene complexes were increasingly used as catalysts for Heck, Suzuki, and Sonogashira reactions, copolymerizations, and aminations of aryl halides.[6] In general, mixtures of imidazolium salts and palladium salts have been used as precatalysts for these reactions. We believe that it is advantageous to use defined palladium(0) carbene complexes, which directly lead to the active palladium(0) complexes without side reactions. In principle, this will allow a more efficient use of the actual catalyst. Despite the increasing use of palladium carbene complexes, there are only a few examples of well-defined palladium(0) carbene complexes known.[7] Of special interest to palladium catalysis would be monocarbenepalladium(0) complexes, which can generate a highly reactive 12e-palladium species. So far, there are only two monocarbenepalladium(0) complexes, **1** and **2**, without additional strongly coordinating phosphine ligands structurally characterized. We thought that complexes **1** and **2** constitute interesting catalysts for coupling reactions of aryl chlorides. Hence, we prepared 1,3-dimesitylimidazol-2-ylidene-palladium(0)-(η^2,η^2)-1,1,3,3-tetramethyl-1,3-divinyl disiloxane **1**[8] by reacting palladium(0)-diallyl ether complex ($Pd_2(dae)_3$)[9] with 1,3-dimesitylimidazol-2-ylidene in the presence of an excess of 1,1,3,3-tetramethyl-1,3-divinyl-disiloxane.[10] The synthesis of (1,3-dimesityl-imidazol-2-ylidene)(naphthoquinone)palladium(0) **2** is achieved by reacting 1 equiv of 1,3-dimesitylimidazol-2-ylidene with (naphthoquinone)Pd(cod)[11] in tetrahydrofuran medium at −78 °C. In addition, (1,3-dimesitylimidazol-2-ylidene)-(benzoquinone)palladium(0) **3** was synthesized in a similar fashion.[8]



1
2

Having prepared the monocarbenepalladium(0) complexes **1**−**3**, we tested the catalytic activity of these complexes for the Heck reaction[12] of aryl chlorides with styrene (Scheme 1, Table 1) and an acrylic ester, respectively (Scheme 2, Table 2).[13] Some preliminary experiments using **3** in common dipolar aprotic solvents such as DMAc in the presence of different bases (Cs_2CO_3, K_3PO_4, NaOAc) have shown that

Scheme 2. Pd-Catalyzed Heck Reaction of Aryl Chlorides with 2-Ethylhexyl Acrylate

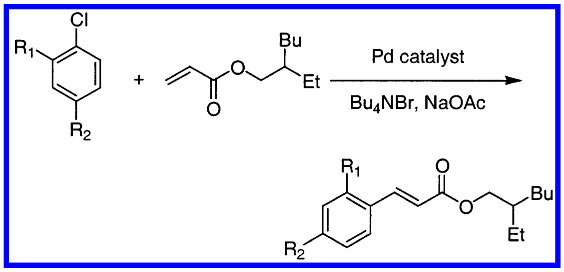


Table 2. Heck Arylation of 2-Ethylhexyl Acrylate in $^nBu_4NBr$

entry	R^1	R^2	catalyst (mol %)	temp (°C)	time (h)	conversion (%)	yield (%)
1	CN	H	**2** (0.5)	140	24	100	99
2	CN	H	**3** (0.5)	140	24	100	97
3	H	NO_2	**2** (0.5)	140	24	100	98
4	H	NO_2	**3** (0.5)	140	24	100	96
5	H	$COCH_3$	**2** (0.5)	140	24	100	99
6	H	$COCH_3$	**3** (0.5)	140	24	100	99
7	H	CF_3	**2** (0.5)	140	24	98	90
8	H	$COCH_3$	**2** (0.5)	140	4	99	98
9	H	$COCH_3$	**2** (0.2)	140	24	100	99
10	H	$COCH_3$	**2** (0.1)	140	24	61	51
11	H	$COCH_3$	**2** (0.1)	140	48	84	74
12	H	$COCH_3$	**2** (0.1)	160	24	80	47
13	H	$COCH_3$	**2** (0.05)	140	24	22	9
14	H	H	**2** (1)	140	48	82	40
15	H	CH_3	**2** (1)	140	48	48	32

only moderate conversions and selectivities could be obtained with activated chloroarenes. A screening of various reaction conditions revealed that simple ionic liquids such as ^{n}Bu$_4$NBr give significantly improved results for this reaction. Ionic liquids are considered "green solvents" due to their high boiling point, low vapor pressure at elevated temperature, and their possible use for extended runs.[14] Tetraalkylammonium salts are the most advantageous ionic liquids due to their low price and availability. Hence, all further reactions were conducted in ^{n}Bu$_4$NBr, which becomes a liquid at reaction temperature.

The three defined monocarbene complexes **1**−**3** were compared in the Heck reaction of both activated and nonactivated chlorobenzenes with styrene in ^{n}Bu$_4$NBr at 140 °C. Complex **1** was found to be thermally unstable and decomposed to palladium black during the catalysis. No decomposition was noticed with complexes **2** and **3** during the catalytic reactions. Activated aryl chlorides such as 4-chloronitrobenzene, 2-chlorobenzonitrile, and 4-chloroacetophenone furnished the corresponding stilbenes in excellent yields (88−99%) in the presence of catalyst **2** or **3**. 4-Chlorobenzotrifluoride gives the desired product in 84−86% yield. Interestingly, the reaction of nonactivated aryl chlorides, e.g., chlorobenzene and 4-chlorotoluene, proceeds with moderate to good yield (67−72%). These reactions constitute one of the successful examples of Heck reactions of nonactivated chloroarenes with styrene in the presence of palladium carbene complexes. The Heck reaction of aryl chlorides was extended to 2-ethylhexyl acrylate in the presence of **2** and **3** as catalysts. Again, activated aryl chlorides (4-chloronitrobenzene, 2-chlorobenzonitrile, 4-chloroacetophenone) provide the corresponding cinnamic esters in excellent yields (97−99%), while 4-chlorobenzotrifluoride yields 90% of the desired product. Chlorobenzene and 4-chlorotoluene gave lower yields, 40 and 32%, respectively, even in the presence of 1 mol % catalyst. Catalyst loading was reduced below 0.5 mol % for activated aryl chlorides. 4-Chloroacetophenone gave 99% yield in the presence of 0.2 mol % catalyst and 74% yield in the presence of 0.1 mol % catalyst. Poor yields were obtained by reducing the catalyst amount below 0.1 mol %.

In summary, we have shown for the first time that defined monocarbenepalladium(0) complexes are suitable catalysts for the palladium-catalyzed Heck reaction of activated and nonactivated aryl chlorides. It is shown that tetraalkylammonium halides constitute superior high-temperature solvents for this type of Heck reaction. This makes this type of catalyst of general interest to industrial fine chemical synthesis.

Acknowledgment. This work has been supported by the state Mecklenburg-Western Pommerania, the Fonds der Chemischen Industrie, and the Bundesministerium für Bildung und Forschung (BMBF). The authors thank Dr. R. Karch (OMG) and Dr. O. Briel (OMG) for general discussions regarding the new palladium complexes. K.S. thanks the Alexander von Humboldt Foundation for a fellowship.

Supporting Information Available: Experimental procedures and characterization data for selected Heck products. This material is available free of charge via the Internet at http://pubs.acs.org.

OL020103H

---

(6) (a) Hillier, A. C.; Nolan, S. N. *Platinum Metals Rev.* **2002**, *46*, 50 and references therein. (b) Herrmann, W. A.; Böhm, V. P. W.; Gstöttmayr, C. W. K.; Grosche, M.; Reisinger, C.-P.; Weskamp, T. *J. Organomet. Chem.* **2001**, *617−618*, 616 and references therein. (c) Done, M. C.; Ruther, T.; Cavell, K. J.; Kilner, M.; Peacock, E. J.; Braussaud, N.; Skelton, B. W.; White, A. *J. Organomet. Chem*. **2000**, *607*, 78. (d) Fürstner, A.; Leitner, A. *Synlett* **2001**, *2*, 290. (e) McGuinness, D. S.; Saendig, N.; Yates, B. F.; Cavell, K. J. *J. Am. Chem. Soc*. **2001**, *123*, 4029. (f) Mathews, C. J.; Smith, P. J.; Welton, T.; White, A. J. P.; Williams, D. J. *Organometallics* **2001**, *20*, 3848. (g) Peris, E.; Loch, J. A.; Mata, J.; Crabtree, R. H. *Chem. Commun*. **2001**, 201.

(7) (a) McGuiness, D. S.; Cavell, K. J.; Skelton, B. W.; White, A. H. *Organometallics* **1999**, *18*, 1596. (b) Böhm, V. P. W.; Gstöttmayr, C. W. K.; Weskamp, T.; Herrmann, W. A. *J. Organomet. Chem*. **2000**, *595*, 186.

(8) (a) Jackstell, R.; Gómez Andreu, M.; Frisch, A.; Selvakumar, K.; Zapf, A.; Klein, H.; Spannenberg, A.; Röttger, D.; Briel, O.; Karch, R.; Beller, M. *Angew. Chem*. **2002**, *114*, 1028; *Angew. Chem., Int. Ed.* **2002**, *41*, 986. (b) Selvakumar, K.; Zapf, A.; Spannenberg, A.; Beller, M. *Chem. Eur. J.* **2002**, in press.

(9) Krause, J.; Cestanic, G.; Haack, K.-J.; Seevogel, K.; Storm, W.; Pörschke, K.-R. *J. Am. Chem. Soc.* **1999**, *121*, 9807.

(10) Arduengo, A. J.; Dias, H. V. R.; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc*. **1992**, *114*, 5530.

(11) (a) Hiramatsu, M.; Fujinami, T.; Sakai, S. *J. Organomet. Chem.* **1981**, *218*, 409. (b) Hiramatsu, M.; Shiozaki, K.; Fujinami, T.; Sakai, S. *J. Organomet. Chem.* **1983**, *246*, 203.

(12) (a) de Meijere, A.; Meyer, F. E. *Angew. Chem*. **1994**, *106*, 2473; *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379. (b) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev*. **2000**, *100*, 3009.

(13) Standard reaction conditions: 1 mmol of aryl chloride, 1.5 mmol of olefin, 1.2 mmol of sodium acetate, catalyst (0.5 mol %), and 2 g of tetrabutylammonium bromide were stirred under argon at 140 °C for 24 h in a Schlenk tube. After the mixture was cooled, the internal standard (diethyleneglycol di-*n*-butyl ether) was added, and the mixture was diluted with 5 mL of water and extracted with 3 × 5 mL of ether. The combined organic layers were dried over sodium sulfate. The conversion and the yield were determined by gas chromatography.

(14) (a) Welton, T. *Chem. Rev*. **1999**, *99*, 2071. (b) Wasserscheid, P.; Keim, W. *Angew. Chem*. **2000**, *112*, 3926; *Angew. Chem., Int. Ed*. **2000**, *39*, 3772.