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Palladaphosphacyclobutenes as catalysts in Heck and Suzuki reactions

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Heck reactions of aryl halides with various olefins and Suzuki reactions of aryl halides with phenylboronic acid catalyzed by palladaphosphacyclobutene have been investigated. The scope of the Heck reaction has been investigated in *N,N*-dimethylacetamide at 140 °C using NaOAc as base. Using 0.1% molar ratio of palladaphosphacyclobuyenes, aryl bromides were converted into 1,2-substitutedethene products in good to high yields through coupling with both vinylarenes and acrylates. Actived aryl chloride reacted with styrene to afford 1,2-substitutedethene products in moderate yields. The scope of the Suzuki reaction has been conducted in toluene at 110 °C using Cs_2CO_3 as base. Using 0.1% molar ratio of palladaphosphacyclobutene, aryl bromides reacted with phenylboronic acid to afford diaryl derivatives in excellent yield. **Copyright © 2008 John Wiley & Sons, Ltd.**

Keywords: palladacycles; Heck coupling; Suzuki coupling; palladaphosphacyclobutenes

Introduction

Palladacycles are recognized as important key intermediates in numerous carbon–carbon (or carbon–heteroatom) bond forming processes and, as such, have been extensively utilized as catalysts.[1] Among these, palladaphosphacycles have emerged as powerful catalysts, allowing the reactions to proceed at low catalyst loading and high turnover numbers (TON). The most used palladaphosphacycles as catalysts are five- or six-membered rings.[2] Four-membered palladaphosphacycles are rather rare[3,4] since their poor stability leads to difficulties in preparation and isolation. Recently, we have successfully developed a method for the synthesis of palladaphosphacyclobutenes, which are air- and heat-stable.[5] Herein we applied this novel type of four-membered palladacycles for Heck and Suzuki reactions.

Results and Discussion

The palladaphosphacyclobutenes **1–4** were prepared by the transmetallation of zirconophosphacyclobutenes with $PdCl_2(MeCN)_2$.[5] The spectroscopic data and the elemental analyses are in agreement with structures depicted in Fig. 1.

Complexes**1–4** were initially tested as catalysts in the Heck reaction. First, we examined the reaction of bromobenzene with styrene in *N,N*-dimethylacetamide (DMA) in the presence of the palladaphosphacyclobutenes **1–4**. Table 1 illustrates the coupling results. Good to excellent yields were obtained in 5 h when 0.1 mol% palladacycle was applied (entries 1–4). Reducing the catalyst loading to 0.01 and 0.001 mol% with longer reaction times also afforded high yields (entries 5 and 6). Interestingly, the palladaphosphacyclobutenes bearing aryl groups in carbon exhibited enhanced catalytic activities (entries 1–3). It is noteworthy that the complexes are not sensitive to oxygen and moisture, and they can be easily managed under atmospheric conditions.

Owing to their catalytic efficacy in the Heck reaction, complex **1** was studied further in the coupling of a number of aryl halides and olefins. The results are summarized in Table 2. The reaction of bromoarene substituted with electron-withdrawing groups can be performed in excellent yield (entry 2) even under 0.001 mol% catalyst loading (entry 3). In the case of deactivated bromoarenes, higher catalyst loading and longer reaction times were required to push the reaction in high yields (entries 4–6). The catalyst effect was also evident for chloroarenes, where only those substituted with electron-withdrawing groups gave reasonable yields in coupling products (entries 12–14). Nonactivated chloroarene gave a low yield in coupling reaction (entry 11).[6] We next investigated the effect of varying the olefins in the Heck reaction using 1-bromobenzene as substrate under the optimized reaction conditions. Styrene led to excellent yields of the desired products (entry 1). Using acrylate led to excellent yields of the desired product (entries 7 and 8). When acrylamide was used, the desired product formed in moderate yield (entry 9). The catalytic system was also active for simple linear alkenes such as oct-1-ene, which led to 1-aryl substituted alkenes as the major product in low yield (entry 10).

Having found that **1** was an excellent catalyst for the Heck reactions, we next examined whether **1** could also facilitate the Suzuki reactions. The reaction of 4-bromoacetophenone with phenylboronic acid under typical Heck reaction conditions, i.e. with 0.1 mol% palladacycle **1** and 1.5 equivalent of NaOAc as base in NMP at 140 °C, gave only a small yield of the desired product, 4-acetylbiphenyl. Changing the conditions to using Cs_2CO_3 as base in toluene as solvent,[7] the yield rose to over 99% (Scheme 1). Both electron-rich and electron-poor aryl bromides could be successfully converted into the desirable products.

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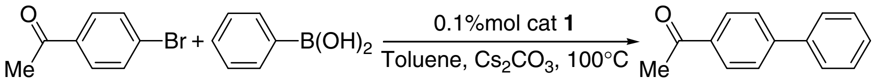
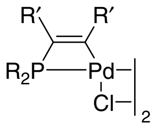


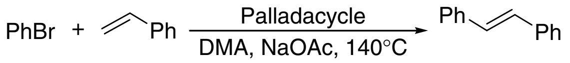
Scheme 1. Palladaphosphacyclobuyene catalyzed Suzuki reaction.



1: R′ = R = Ph,
2: R′ = *p*-Tol, R = Ph
3: R′ = Ph, R = *i*-Pr
4: R′ = *n*-Bu, R = Ph

Figure 1. Palladaphosphacyclobutenes.

Table 1. Palladacycle-catalyzed Heck reaction



Entry	Palladacycle	mol % cat	t (h)	yield (%)
1	**1**	0.1	5	95
2	**2**	0.1	5	89
3	**3**	0.1	5	92
4	**4**	0.1	5	63
5	**1**	0.01	10	89
6	**1**	0.001	24	56

The representative results were summarized in Table 3. In all runs, the biphenyl was only obtained as a minor byproduct (less 2%). Other palladacycles **2–4** could also be used as catalysts for the Suzuki reaction and exhibited similar yields.

Conclusions

It can be concluded that palladaphosphacyclobutenes can be used as catalysts for carbon–carbon bond formation through Heck and Suzuki reactions. Using 0.1% molar ratio of palladaphosphacyclobutenes, aryl bromides were converted into 1,2-substitutedethene products in good to high yields through coupling with both vinylarenes and acrylates. Aryl bromides reacted with phenylboronic acid to afford diaryl derivatives in excellent yield.

Experimental

General

All manipulations were conducted in Schlenk tubes and under nitrogen with a slight positive pressure. GC analyses were preformed on a gas chromatograph equipped with a flame ionization detector using a capillary column (CBP1-M25-025). The GC yields were determined using suitable hydrocarbons as internal standards. Unless otherwise noted, all starting materials were commercially available and were used without further purification. ^{1}H NMR and ^{13}C NMR spectra were recorded on Jeol 300 NMR spectrometer with TMS as internal standard.

General procedure for the synthesis of palladaphosphacyclobutenes 1–4

All the palladaphosphacyclobutene were prepared according to the literature method.[5] Herein only the synthesis of

Table 2. Heck reaction of aryl bromide with olefin using catalyst **1**[a]

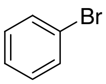
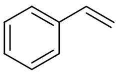
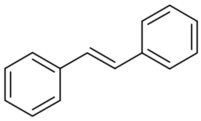
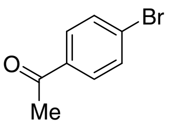
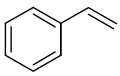
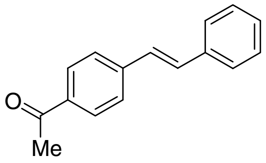
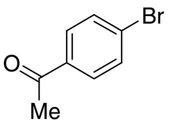
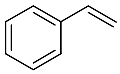
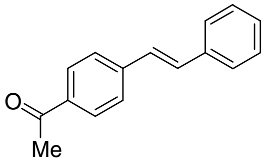
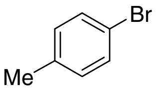
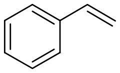
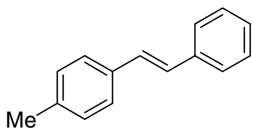
Entry	Aryl bromide	Olefin	Time (h)	Cat. mol%	Product	Yield (%)[b]	TON[c]
1	 Br		5	0.1		95	950
2	 Br O Me		5	0.01	 O Me	>99 (92)	9900
3	 Br O Me		10	0.001	 O Me	98	98000
4	 Br Me		10	0.1	 Me	84 (77)	840

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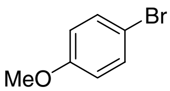
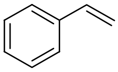
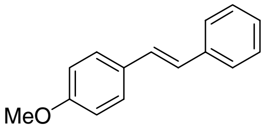
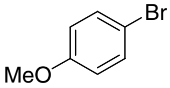
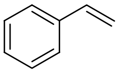
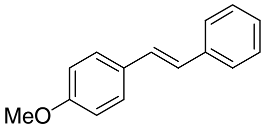
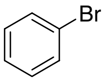
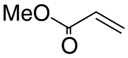
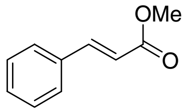
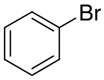
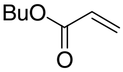
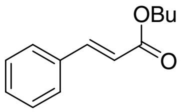
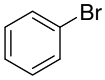
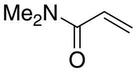
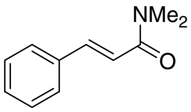
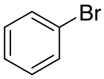
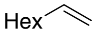
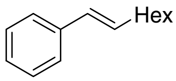
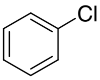
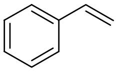
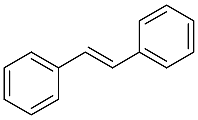
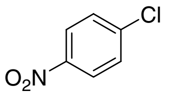
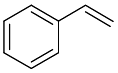
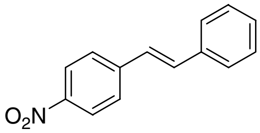
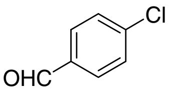
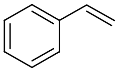
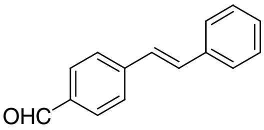
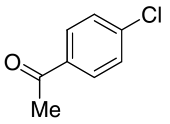
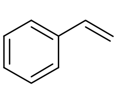
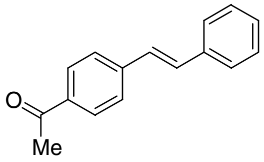
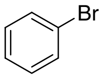
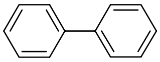
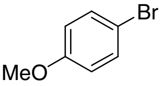
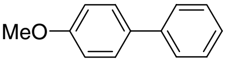
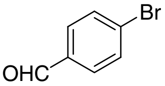
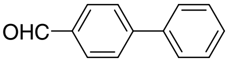
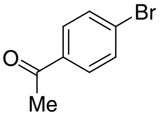
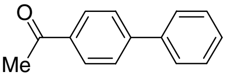
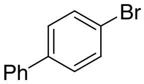
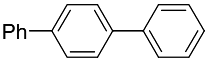
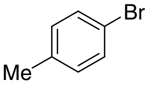
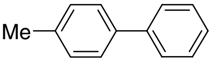
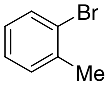
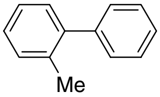
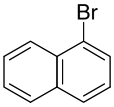
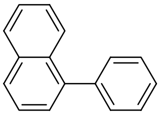
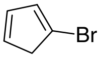
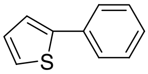
Table 2. (*Continued*)

Entry	Aryl bromide	Olefin	Time (h)	Cat. mol%	Product	Yield (%)[b]	TON[c]
5			10	0.1		24 (15)	240
6			10	0.5		98 (94)	196
7			24	0.1		90 (53)[d]	900
8			24	0.1		93 (62)[d]	930
9			24	0.1		41 (33)	410
10			24	0.1		33 (26)	330
11			24	1		15	15
12			24	0.1		41 (30)	410
13			24	0.1		76	760
14			24	0.1		71	710

[a] Reaction conditions: aryl bromide (1 mmol), olefin (1.5 mmol), NaOAc (1.5 mmol), DMA (5 ml), catalyst 1.
[b] NMR yields, isolated yields are given in parentheses.
[c] TON = mol of product/mol of the catalyst.
[d] The products were partially hydrolyzed to form acid after workup.

palladaphosphacyclobutene**1** is described in detail as an example. [2-(Dicyclopentadienylchlorozircono)-1,2-diphenylvinyl] diphenylphosphine (248 mg, 0.4 mmol), $PdCl_2(CH_3CN)_2$ (104 mg, 0.4 mmol) and THF (5 ml) were added to the Schlenk tube, and the mixture was stirred for 2 h at 50 °C. Palladaphosphacyclobutene **1** was formed exclusively. ^{31}P NMR δ −82.6 (81 MHz, THF, 85% H_3PO_4). Removal of the solvent and crystallization in $ClCH_2CH_2Cl$(DCE) at 80 °C afforded 168 mg of the compound **1** as a yellow solid (isolated yield 83%). M.p. 270 °C (decomp.). ^1H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 6.88–7.86 (m); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si) δ 126.8–133.7 (m, sp^2 carbon); ^{31}P NMR (81 MHz, $CDCl_3$, 85% H_3PO_4) δ −83.4; positive ion ESI-MS: 469.0.

Table 3. Suzuki reaction of aryl bromide with phenylboronic acid using complex **1** as catalyst[a]

Entry	Aryl bromide	Time (h)	Product	Yield (%)[b]	TON[c]
1		48		>99	990
2		24		>99 (98)	990
3		24		>99 (84)	980
4		24		>99	990
5		24		>99	990
6		48		>99	990
7		48		(96)	960
8		24		(95)	950
9		48		98	980

[a] Reaction conditions: aryl bromide (1 mmol), phenylboronic acid (1.2 mmol), Cs_2CO_3 (1.0 mmol), toluene (5 ml), catalyst **1**.
[b] NMR yields, isolated yields are given in parentheses.
[c] TON = mol of product/mol of the catalyst.

Heck reaction

General procedure

Under nitrogen atmosphere, NaOAc (1.5 mmol), olefin (1.5 mmol) and aryl bromide (1 mmol), DMA (5 ml) was added in turn to a Schlenk tube equipped with a magnetic stirring bar. A 0.001–0.01 mol/l catalyst in NMP solution was added to the Schlenk tube. The mixture was stirred at 140 °C and monitored by GC. After 5–24 h, the reaction mixture was quenched with 1 M HCl and extracted with a mixture of ethyl acetate and petroleum ether (2 : 3). The organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using petroleum ether or mixture of petroleum ether and ethyl acetate.

Suzuki reaction

General procedure

Aryl halide (1.0 mmol), benzeneboronic acid (1.2 mmol), cesium carbonate (1.0 mmol) and toluene (3 ml) were added to the Schlenk tube. Catalyst, 0.01 mol/l, in NMP solution was added to the Schlenk tube. The mixture was stirred at 100 °C. After the reaction had completed, the mixture was quenched with water and extracted with ethyl ether. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using petroleum ether or mixture of petroleum ether and dichloromethane.

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References

[1] M. Albrecht, G. van Koten, *Angew. Chem. Int. Edn* **2001**, *40*, 3750; b) R. B. Bedford, *Chem. Comunn.* **2003**, 1787; c) R. B. Bedford, C. S. J. Cazin, D. Holder, *Coord. Chem. Rev.* **2004**, *248*, 2283; d) J. Dupont, C. S. Consorti, J. Spencer, *Chem. Rev.* **2005**, *105*, 2527; e) W. A. Herrmann, C. Brossmer, K. Öfele, C.-P. Reisinger,

T. Priermeier, M. Beller, H. Fischer, *Angew. Chem., Int. Ed.* **1995**, *34*, 1844; f) D. A. Albisson, R. B. Bedford, S. E. Lawrence, P. N. Scully, *Chem. Commun.* **1998**, 2095; g) M. Ohff, A. Ohff, D. Milstein, *Chem. Commun.* **1999**, 357; h) H. Weissman, D. Milstein, *Chem. Commun.* **1999**, 1901; i) D. A. Alonso, C. Nájera, M. C. Pacheco, *Org. Lett.* **2000**, *2*, 1823; j) D. S. McGuinness, K. J. Cavell, *Organometallics* **2000**, *19*, 741; k) J. Dupont, A. S. Gruber, G. S. Fonseca, A. L. Monteiro, G. Ebeling, *Organometallics* **2001**, *20*, 171; l) S. Gibson, D. F. Foster, G. R. Eastham, R. P. Tooze, D. J. Cole-Hamilton, *Chem. Commun.* **2001**, 779; m) R. B. Bedford, S. L. Welch, *Chem. Commun.* **2001**, 129; n) M. S. Viciu, R. A. Kelly, III, E. D. Stevens, F. Naud, M. Studer, S. P. Nolan, *Org. Lett.* **2003**, *5*, 1479; o) H. Weissman, D. Milstein, *Chem. Commun.* **1999**, 1901; p) D. A. Alonso, C. Nájera, M. C. Pacheco, *Org. Lett.* **2000**, *2*, 1823; q) A. S. Gruber, D. Zim, G. Ebeling, A. L. Monteiro, J. Dupont, *Org. Lett.* **2000**, *2*, 1287; r) M. T. Reetz, J. G. Vries de, *Chem. Commun.* **2004**, 1559; s) A. H. M. Vries de, J. M. C. A. Mulders, J. H. M. Mommers, H. J. W. Henderickx, J. G. Vries de, *Org. Lett.* **2003**, *5*, 3285; t) C. Zhang, J. Huang, M. L. Trudell, S. P. Nolan, *J. Org. Chem.* **1999**, *64*, 3804; u) I. P. Beletskaya, A. V. Cheprakov, *J. Organomet. Chem.* **2004**, *689*, 4055; v) Z. Xiong, N. Wang, M. Dai, A. Li, J. Chen, Z. Yang, *Org. Lett.* **2004**, *6*, 3337; w) C. S. Consorti, M. L. Zanini, S. Leal, G. Ebeling, J. Dupont, *Org. Lett.* **2003**, *5*, 983.

[2] J. Dupont, M. Pfeffer, J. Spencer, *Eur. J. Inorg. Chem.* **2001**, 1917; b) A. C Cope, E. C. Friedrich, *J. Am. Chem. Soc.* **1968**, *90*, 909; c) H. Alper, *J. Organomet. Chem.* **1973**, *61*, C62; d) J. Dehand, A. Mauro, H. Ossor, M. Pfeffer, R. H. D. Santos, J. R. Lechat, *J. Organomet. Chem.* **1983**, *250*, 537; e) H. M. McPherson, J. L. Wardell, *Inorg. Chim. Acta.* **1983**, *75*, 37.

[3] D. Sole, L. Vallverdu, X. Solans, M. Font-Bardia, J. Bonjoch, *J. Am. Chem. Soc.* **2003**, *125*, 1587; b) J. Dupont, N. R. Basso, M. R. Meneghetti, R. A. Konrath, R. Burrow, M. Horner, *Organometallics* **1997**, *16*, 2386.

[4] R. Arnek, K. Zetterberg, *Organometallics*, **1987**, *6*, 1230; b) D. Carmichael, P. B. Hitchcock, J. F. Nixon, F. Mathey, L. Ricard, *J. Chem. Soc., Chem. Commun.*, **1989**, 1389; c) Y. Agnus, M. Gross, M. Labarelle, R. Louis, B. Metz, *J. Chem. Soc., Chem. Commun.*, **1994**, 939; d) W. Henderson, A. G. Oliver, C. E. F. Rickard, L. J. Baker, *Inorg. Chim. Acta* **1999**, *292*, 260.

[5] X. Yan, C. Xi, *Organometallics*, **2008**, *27*, 152.

[6] A. F. Littke, G. C. Fu, *Angew. Chem., Int. Edn* **2002**, *41*, 4176.

[7] M. J. Sharp, V. Snieckus, *Tetrahedron Lett.* **1985**, *26*, 5997; b) T. Watanabe, N. Miyaura, A. Suzuki, *Synlett* **1992**, 207; c) A. Suzuki, *Pure Appl. Chem.* **1994**, *66*, 213; d) J. C. Anderson, H. Namli, *Synlett.* **1995**, 765; e) J. C. Anderson, H. Namli, C. A. Roberts, *Tetrahedron* **1997**, *53*, 15123; f) S. Nerdinger, C. Kendall, R. Marchhart, P. Riebel, M. R. Johnson, C.-F. Yin, L. D. Eltis, V. Snieckus, *J. Chem. Soc., Chem. Commun.* **1999**, 2259.

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