Preparation of polyaniline with a monolayer of colloidal silica*:* To control the morphology of the polymer, a monolayer of close packed colloidal silica (0.5 μm diameter standard silica spheres obtained from Duke Scientific, Palo Alto, California) was first deposited on the Pt substrate. After the Pt plate was rinsed with the SDS solution, a droplet of a colloidal silica solution containing 0.4 wt. % silica particles was placed on the Pt substrate. The SDS treatment improved the wetting behavior of the silica colloidal solution and allowed the droplet to spread over the whole surface of the Pt plate. The excess solution was removed from the substrate by positioning the Pt plate vertically to allow the excess water to flow off. After drying, the Pt plate with the silica particles was heated in an oven at 110 °C for 0.5 h. Electrochemical deposition of polyaniline was conducted using the same procedure.

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A New Generation of Air Stable, Highly Active Pd Complexes for C–C and C–N Coupling Reactions with Aryl Chlorides[**]

Anita Schnyder, Adriano F. Indolese,[*]
Martin Studer,[*] and Hans-Ulrich Blaser

Palladium-catalyzed coupling reactions such as the Suzuki coupling, the Heck reaction, and the Buchwald–Hartwig amination or arylation of ketones are now standard transformations in both academic and industrial laboratories.[1] While simple palladium salts are excellent catalysts for reactive substrates, such as aryl iodides, activated aryl bromides, or aromatic diazo compounds, the less reactive but commercially very interesting aryl chlorides require palladium catalysts activated and stabilized by additional ligands. A crucial factor for a successful catalyst is the choice of the right ligand, most frequently an electron-rich, bulky tertiary phosphane, and in recent years a number of very effective ligands have been developed for the reactions mentioned above.[2]

However, these customized phosphanes are usually expensive and their synthesis can be difficult, often involving multistep syntheses using air-sensitive substances. An interesting alternative could be secondary phosphanes, many of which are available in bulk quantities at a relatively low price. Even though their application in transition-metal catalysis is rare,[3] we recently found that secondary dialkyl phosphanes such as HP(*tert*-butyl)$_2$ and HP(adamantyl)$_2$ can indeed be applied successfully for the palladium-catalyzed Heck reaction even with notoriously unreactive, electron-rich aryl chlorides.[4]

This result encouraged us to investigate other palladium-catalyzed reactions (Scheme 1) using a combinations of palladacycles and secondary phosphanes. Palladacycles have recently been described as versatile catalyst precursors for a number of coupling reactions[5] and they can be regarded as stable, easily accessible aryl palladium species. Catalyst libraries with high diversity could readily be prepared with this strategy since a wide variety of palladacycles and secondary phosphanes are available.

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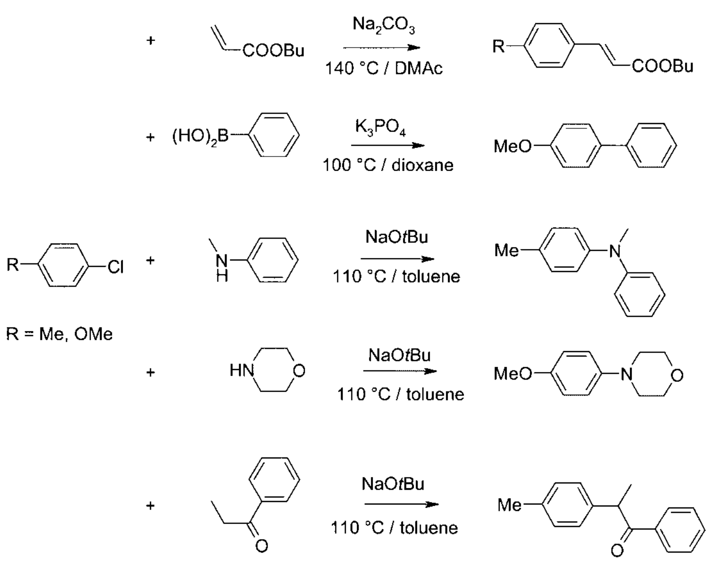
Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.



Scheme 1. Substrates and conditions used for coupling reactions catalyzed by palladacycle/secondary phosphane catalysts.

Herein we report very active catalysts obtained in situ from palladacycles and secondary phosphanes for the Heck and Suzuki reaction, the Buchwald–Hartwig amination, and the α-arylation of ketones with aryl chlorides as the arylating agent. In addition, the isolated and well-characterized palladacycle/HPR$_2$ complexes are stable, easy to handle, and versatile catalysts for these transformations.

For a first screening we selected the reaction of phenylboronic acid with 4-chloroanisole, and assembled a small catalyst library prepared in situ by mixing the five palladacycles **1**–**5** and three sterically demanding dialkyl phosphanes (Scheme 2; HPCy$_2$, HPNor$_2$ and **6**[6]). The palladacycles are easily accessible by orthometalation of substituted benzenes containing a coordinating N or O atom to form five- or six-membered chelating rings.[5] All combinations gave active catalysts, thus showing the basic suitability of our approach, whereas the palladacycles alone yielded less than 2% coupling product (Figure 1 and Table 1[7]). Some trends were clearly visible: Conversions generally improved going from the least demanding ligand **6** to the bulkiest phosphane HPNor$_2$; the highest yields (>90%) were obtained with **1**, **2**, and **5** in combination with HPNor$_2$. The combination **1**/HPNor$_2$ rendered a particularly active catalyst where 95% of the starting material reacted within the first hour, while conversion with all other catalytic systems after 1 h never exceeded 50%.

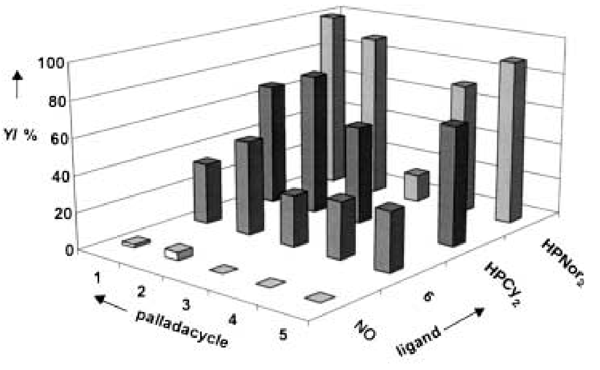
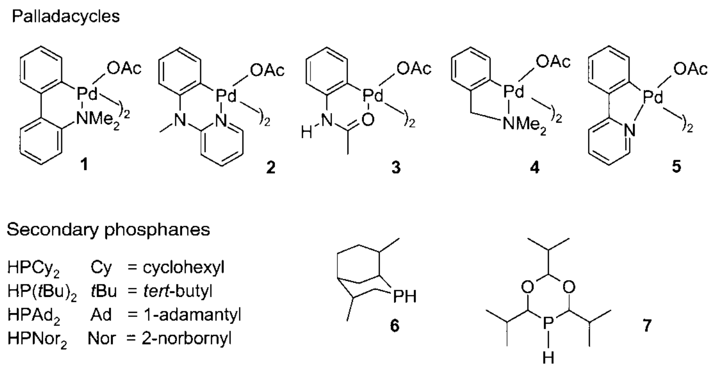


Figure 1. GLC yields (Yl[%]) of the Suzuki coupling of 4-chloroanisole with phenylboronic acid in the presence of palladacycles **1**–**5** and selected secondary phosphanes.[7]

Table 1. GLC yields for the Suzuki and Heck reaction for various combinations of Pd precursors and secondary phosphanes.[7]

Entry	Ligand	Suzuki **1** (1%)	Heck **1** (0.5%)[a]	Heck **3** (0.5%)	Heck **4** (0.5%)	Heck[4] PdCl$_2$ (1%)	Heck[4] Pd(OAc)$_2$ (0.5%)
1	–	2%	0%	0%	0%	0%	0%
2	PCy$_3$	53%	19%	24%	22%	40%	15%
3	HPCy$_2$	67%	32%	30%	35%	39%	17%
4	HPNor$_2$	100%	41%	40%	45%	77%	34%
5	HPAd$_2$	84%	58%	74%	65%	78%	52%
6	HP(*t*Bu)$_2$	94%	46%	71%	77%	77%	53%
7	**6**	33%	4%	15%	0%	n.a.	n.a.
8	**7**	61%	20%	37%	18%	n.a.	n.a.
9	P(*t*Bu)$_3$	n.a.	61	70%	71%	98%	49%

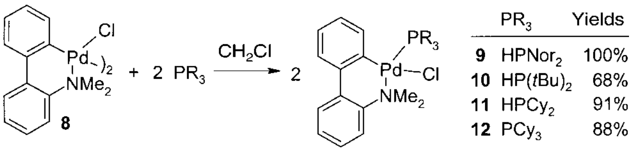
Conditions: See Scheme 1, reaction time 20 h; [a] average of 2 runs. n.a. = not available.



Scheme 2. Structures and numbering of palladacycles and secondary phosphanes.

Similar screening experiments with palladacycles **1**, **3**, and **4**, PdCl$_2$, and Pd(OAc)$_2$ were also carried out for the Heck reaction of 4-chloroanisole with *n*-butyl acrylate, and gave similarly encouraging results (Table 1). For both the Suzuki and the Heck reaction, these in situ catalysts have similar activity as the [Pd$_2$(dba)$_3$]/P(*t*Bu)$_3$ (dba = *trans*,*trans*-dibenzylideneacetone) catalysts developed by Littke and Fu.[8] It is interesting to note that whereas HPNor$_2$ is the preferred ligand for the Suzuki coupling, HPAd$_2$ and H(*t*Bu)$_2$ give the highest conversion for the Heck reaction. It is precisely this catalyst specificity which makes the combinatorial approach attractive because it guarantees access to a broad range of different Pd complexes and enables the optimal one to be found as fast as possible.

While the in situ approach is very useful for catalyst screening, for preparative purposes it would be more attractive to have one or at most a few one-component catalysts with high activities for as many C–C and C–N coupling reactions as possible. On the basis of our screening results and some additional experiments, we decided that palladacycle **1** in combination with the phosphanes depicted in Scheme 2 would give us a fair chance to reach this goal. Indeed we succeeded in developing a simple procedure to obtain isolated complexes **9**–**12** by treating the chloride-bridged palladacycle **8** with several basic phosphanes in high yields[9] (Scheme 3).



	PR$_3$	Yields
9	HPNor$_2$	100%
10	HP(tBu)$_2$	68%
11	HPCy$_2$	91%
12	PCy$_3$	88%

Scheme 3. Structure, yield, and numbering of the isolated palladacycles.

Table 2 summarizes the results of the screening program with the four isolated palladacycles **9**–**12** in the five model reactions depicted in Scheme 1. Complex **12** was included as a reference because PCy$_3$ has been shown to be one of the most effective ligands known for these reactions.[10] Without discussing these results in too much detail, it is important to note that in each reaction one of the new complexes—but not always the same one—gives either comparable or better results than the PCy$_3$ complex. In the Suzuki reaction with 0.1 mol% **9**, 660 turnovers were achieved in 20 h; these catalytic activities are comparable to screening results recently described by Bedford and Cazin[11] using a combination of a palladacycle of type **4** in combination with PCy$_3$. This publication appeared during the course of our work and also reported that catalysts formed in situ have a similar performance as the isolated complexes. In addition, it was shown that under optimal reaction conditions (especially replacement of K$_3$PO$_4$ with the more expensive Cs$_2$CO$_3$) this catalyst type is capable of achieving up to 8000 turnovers with 4-chloroanisole. For the Heck reaction, our palladacycles are comparable or more active than the most active catalysts reported in the literature, [Pd(dba)$_2$]/P(nBu)Ad$_2$[12] and Pd(OAc)$_2$/HPAd$_2$.[4] An interesting result was recently published using oxime-derived palladacycles which catalyzed Heck reactions between nonactivated aryl chlorides and methyl acrylate or styrene in the absence of any phosphane with turnovers around 100.[13] Our results for the arylation and amination reactions also compare well with those obtained by Buchwald and co-workers[14] and Kawatsura and Hartwig[15] using electron-rich tertiary phosphanes with a biphenyl and ferrocenyl backbone, respectively.

Table 2. GLC yields for various coupling reaction using isolated palladacycles **9–12**.[7]

Complex	Ligand	Suzuki (1%)	Heck (1%)	Heck (0.25%)	Arylation (0. 5%)	Amination[a] (0.5%)	Amination[b] (2%)
9	HPNor$_2$	95	100	48	100	100	100
10	HP(tBu)$_2$	45	100	46	60	94	100
11	HPCy$_2$	91	100	89	69	98	82
12	PCy$_3$	99	95	42	99	66	38

Reaction conditions: See Scheme 1, reaction time for Suzuki and Heck: 20 h; for arylation and amination 15 h. [a] *N*-methylaniline substrate. [b] Morpholine substrate.

The mode of action and the nature of the active species of the palladacycle/secondary phosphane catalysts are not yet known.[4] In a stoichiometric reaction of palladacycle **1** with HPCy$_2$ we obtained low yields of 2-dimethylamino-2′-dicyclohexylphosphanylbiphenyl, previously described by Buchwald and co-workers[14a] as a very effective ligand for both the Suzuki coupling and the Buchwald–Hartwig amination. However, we doubt that the catalytic activity of our novel catalysts is really a consequence of this species because—among other observations—we found that this ligand is not active for the Heck reaction.[16]

In conclusion, we have developed a new type of highly active Pd catalysts consisting of a palladacycle and a secondary phosphane with broad applicability for various coupling reactions. Very high yields can be obtained for the Suzuki coupling, the Heck reaction, the Buchwald–Hartwig amination as well as the ketone arylation by using aryl chlorides as starting materials. The catalysts can either be prepared in situ starting from a palladacycle and a secondary phosphane thereby allowing a combinatorial screening approach or the isolated preformed complex can be used which is very convenient for preparative purposes and also in chemical production. We believe that palladacycle **9**[17] is at the moment the most practical catalyst, with the broadest application range, for use in the laboratory, but in principle it is possible to prepare complexes with any combination of palladacycle and secondary phosphane.

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[7] Synthetic procedures: General: Usually, only GLC yields were determined (internal standard). Where investigated, the yields of the isolated products were in a comparable range.[4] *Suzuki reaction*: Phenylboronic acid (1.5 mmol), 4-chloroanisole (1 mmol), and K_3PO_4 (3 mmol) in dioxane (2 mL) were heated to 100 °C. A solution of the catalyst was prepared by mixing the palladacycle (0.01 mmol Pd) with a solution of the ligand (0.015 mmol) in dioxane (0.2 mL), and it was added to the hot reaction mixture. The reaction mixture was stirred for 20 h. Samples were withdrawn by syringe and analyzed by GLC. *Heck reaction*: Sodium carbonate (7.5 mmol) was placed in a Schlenk tube under argon. Degassed *N*,*N*-dimethylacetamide (DMAc, 4 mL), 4-chlorotoluene (5 mmol), butyl acrylate (7.5 mmol), and diethylene glycol dibutyl ether (internal standard) were added, and the reaction mixture was heated to 140 °C. A solution of the catalyst **1** (0.1 mmol) in DMAc (1 mL) was added by syringe to the hot reaction mixture. The reaction mixture was stirred for 20 h. After cooling the reaction mixture to room temperature, it was partitioned between diethyl ether and water, and the organic phase was analyzed by GLC. *Arylation reaction*: NaO*t*Bu (3.9 mmol) was placed in a Schlenk tube under argon. Degassed toluene (3 mL), 4-chlorotoluene (3 mmol), and propiophenone (3.6 mmol) were added, and the reaction mixture was stirred for 30 minutes at room temperature. It was then heated to 110 °C, and a solution of the catalyst **1** (0.06 mmol) in toluene (1 mL) was added by syringe to the hot reaction mixture. The reaction mixture was stirred for 15 h. After cooling the reaction mixture to room temperature, it was partitioned between *tert*-butyl methyl ether (TBME) and water, and the organic phase was analyzed by GLC. *Amination reactions*: NaO*t*Bu (4.2 mmol) was placed in a Schlenk tube under argon. Degassed toluene (3 mL), aryl chloride (3 mmol), and amine (3.6 mmol) were added, and the reaction mixture was stirred for 30 min at room temperature. It was then heated to 110 °C, and a solution of the catalyst **1** (0.06 mmol) in toluene (1 mL) was added by syringe to the hot reaction mixture. The reaction mixture was stirred for 15 h. After cooling the reaction mixture to room temperature, it was partitioned between TBME and water, and the organic phase was analyzed by GLC.

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[9] General procedure: Complexes **9**–**12** were easily prepared by adding the appropriate phosphane to a degassed suspension of the dimeric palladacyclic chloride **8** in dichloromethane under argon. The resulting complexes are soluble and the solutions are stable against hydrolysis and oxidation by air. Some metallic palladium was removed by filtering the solution through a plug of silica. The solutions were concentrated to a minimal volume and the complexes precipitated with hexane. Complexes **9**–**12** were obtained as yellow to brownish yellow powders in medium to high yields that were completely odorless and air stable for at least several months. (For details see the Supporting Information).

[10] Unfortunately, the complex with the best ligand, $P(tBu)_3$[7], was not stable and could not be isolated.

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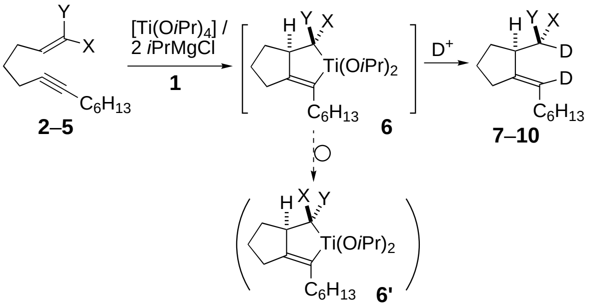
[17] This complex is commercially available in laboratory quantities from Strem and in technical quantities from Solvias AG.

Sulfur-Functionalized Olefins for Titanacycle Formation: Tandem Asymmetric Cyclization and the Pummerer Reaction Based on Sulfoxides Promoted by Titanium(II)-to-Titanium(IV) Relay**

Miho Narita, Hirokazu Urabe, and Fumie Sato*

Sulfur functional groups such as sulfides, sulfoxides, and sulfones have found numerous and pivotal applications in organic synthesis.[1] When enynes having a sulfur functional group are subjected to cyclization mediated by (stoichiometric) group-four transition metals,[2,3] the formation of new sulfur-functionalized metallacycles is expected and their behavior should be of considerable interest. Considering that study along this line is so far notably limited,[4] we report here new aspects of the use of vinylic sulfur functional groups in the titanium alkoxide-mediated enyne cyclization.

First, the viability of the cyclization of enynes having a vinylic sulfide, sulfone, or sulfoxide moiety with a $\mathrm{Ti^{II}}$ alkoxide reagent, $[Ti(OiPr)_4]/2\,iPrMgCl$ (**1**),[3] was briefly surveyed [Eq. (1)].



(1)

The *E*- and *Z*-vinyl sulfides **2** and **3** underwent clean and, more importantly, stereospecific and stereoselective cyclization to the most likely titanacycles **6**, which underwent deuteriolysis to give the isomeric deuterated products **7** and **8**, respectively [Eq. (1) and entries 1 and 2, Table 1].[5,6] Analogously, the *E*-vinyl sulfone **4** afforded **9** (entry 3) upon deuteriolysis, which suggests the selective generation of the titanacycle **6**. Contrarily, the *Z*-vinyl sulfone **5** gave a mixture of **10** (minor constituent) and **9** (as a major component; entry 4), which indicates that the stereochemical integrity of **5**

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