DOI: 10.1002/chem.201002386

Well-Defined Air-Stable Palladium HASPO Complexes for Efficient Kumada–Corriu Cross-Couplings of (Hetero)Aryl or Alkenyl Tosylates

Lutz Ackermann,*[a] Anant R. Kapdi,[a] Sabine Fenner,[a] Christoph Kornhaaß,[a] and Carola Schulzke[b]

Abstract: Palladium complexes of representative *h*etero*a*tom-substituted *s*econdary *p*hosphine *o*xide (HASPO) preligands were synthesized and fully characterized, including X-ray crystal structure analysis. Importantly, these well-defined complexes served as highly efficient catalysts for Kumada–Corriu cross-coupling reactions of aryl, alkenyl, and even heteroaryl tosylates. Particularly, an air-stable catalyst derived from inexpensive PinP(O)H displayed a remarkably high catalytic efficacy, which resulted in cross-couplings at low catalyst loadings under exceedingly mild reaction conditions with ample scope.

Keywords: catalysis · cross-coupling · ligand · palladium · tosylate

Introduction

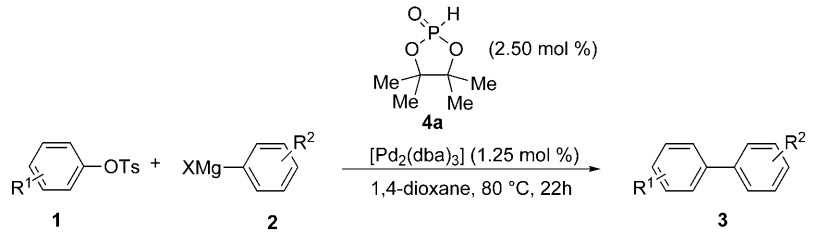
Transition-metal-catalyzed cross-coupling reactions between organic halides and organometallic or main-group-element nucleophiles are among the most valuable tools for regioselective C–C bond formations.[1,2] Due to their mild reaction conditions, these transformations found widespread applications in various research areas, such as crop protection, material sciences, or medicinal chemistry. Traditionally, aryl iodides, triflates, bromides, and more recently chlorides[3,4] served as organic electrophiles for the regioselective synthesis of substituted (hetero)arenes.[3,5] On the contrary, the use of aryl or alkenyl tosylates in cross-coupling chemistry is highly desirable, since they can be prepared from readily available phenols or ketones using inexpensive reagents, and because they are usually highly crystalline as well as stable towards hydrolysis.[3] Unfortunately, the remarkable stability of these user-friendly electrophiles translates into a significantly diminished reactivity in metal-catalyzed coupling reactions. As a result, palladium-catalyzed functionalizations of electronically unactivated aryl tosylates usually required the use of specifically designed stabilizing ligands.[3,6] Thus far, this ligand design mainly focused on electron-rich tertiary phosphines, which can be prone to undergo oxidation. Specifically, generally applicable palladium-catalyzed cross-coupling reactions between organomagnesium reagents and unactivated aryl tosylates were elegantly accomplished with a palladium complex derived from an electron-rich analogue of the Josiphos ligand.[7–9] Unfortunately, heterocyclic[10] tosylates bearing Lewis-basic nitrogen-containing functionalities proved to be detrimental to the catalytic activity of the Josiphos-based palladium complex.[7,8] We, on the contrary, devised an in situ generated catalyst of air-stable *h*etero*a*tom-substituted[11] *s*econdary *p*hosphine *o*xide (HASPO)[12] preligands for challenging arylations of inter alia aryl bromides, chlorides, and fluorides,[13] which notably proved to be amenable to Kumada-Corriu coupling reactions of unactivated aryl tosylates as well.[14] Thus, particularly complexes generated from inexpensive PinP(O)H (**4a**) displayed a high catalytic activity (Scheme 1), even when using more demanding Lewis-basic N-heteroaromatic tosylates.

Despite this remarkable recent progress in the use of HASPO preligands for catalytic cross-coupling reactions,[12–14] the coordination chemistry of catalytically relevant HASPOs has thus far not been explored. Moreover, structurally characterized HASPO complexes have, to the best of our knowledge, previously not been employed as well-defined catalysts for cross-coupling reactions.[12] Therefore, we became interested in preparing novel isolated HASPO transition-metal complexes and in probing their performance in catalytic arylation reactions. As a result of our efforts, we disclose herein the synthesis of fully characterized palladium complexes of representative HASPO preligands and their use as catalysts in challenging Kumada–Corriu cross-coupling reactions of unactivated aryl and heteroaryl tosylates. Importantly, these studies also represent a first application of secondary phosphine oxides as preligands for cross-couplings of alkenyl tosylates.

[a] Prof. Dr. L. Ackermann, Dr. A. R. Kapdi, Dipl.-Chem. S. Fenner, Dipl.-Chem. C. Kornhaaß
Institut für Organische und Biomolekulare Chemie
Georg-August-Universität
Tammannstrasse 2, 37077, Göttingen (Germany)
Fax: (+49) 551-39-6777
E-mail: lutz.ackermann@chemie.uni-goettingen.de

[b] Dr. C. Schulzke
School of Chemistry, Trinity College Dublin
College Green, Dublin 2 (Ireland)

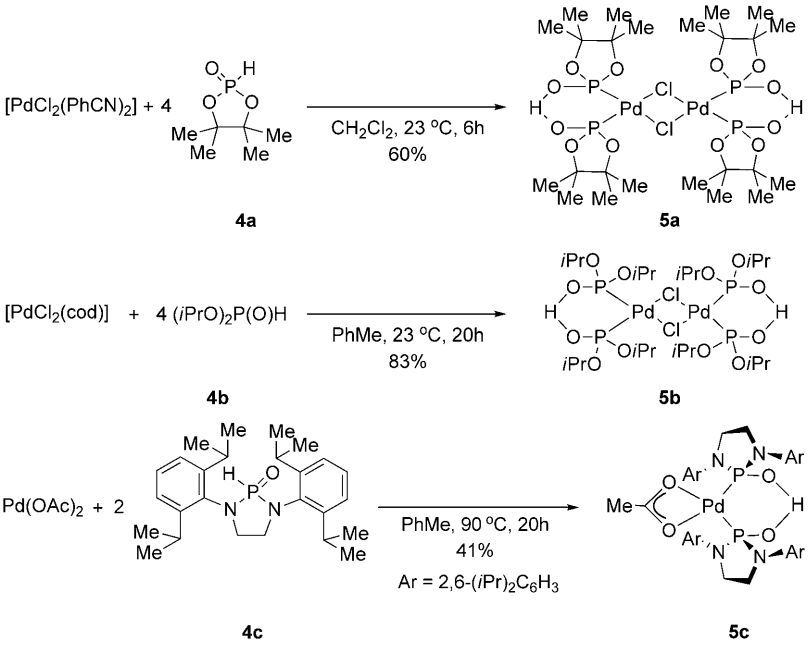
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201002386.



Scheme 1. Kumada–Corriu cross-coupling of aryl tosylates **1** with an in situ generated complex of HASPO preligand **4a**.

Results and Discussion

Cross-couplings of alkenyl tosylates with an in situ generated catalytic system: In situ generated transition-metal complexes of air-stable (HA)SPO preligands were thus far solely employed for cross-coupling reactions of *aryl* sulfonates.[12] Therefore, we probed at the outset of our studies the application of the in situ generated catalytic system of PinP(O)H (**4a**) for the diastereoselective synthesis of tri- and tetrasubstituted alkenes **3** (Table 1). Thereby, a variety of differently substituted alkenes **3** was accessed with excellent chemoselectivities (Table 1, entries 1–12). Importantly, the catalytic system turned out not to be limited to cyclic alkenyl tosylates **1**, but also enabled the efficient and selective synthesis of acyclic olefins **3am** and **3an** (Table 1, entries 13, and 14).



Scheme 2. Synthesis of novel HASPO palladium complexes **5a**–**5c**.

Synthesis of well-defined palladium complexes: Despite the outstanding catalytic activity and wide applicability exerted by in situ generated HASPO complexes, the coordination chemistry of catalytically relevant derivatives has thus far not been explored.[12] Therefore, we set out to prepare well-defined palladium complexes **5a**–**5c** by employing representative air-stable preligands **4a**–**4c** (Scheme 2).

Importantly, the molecular structures of homobimetallic complex **5b** and monometallic complex **5c** revealed the hydrogen-bond stabilized nature of the quasi-bidentate ligand (Figure 1 and 2, respectively).[15] Furthermore, it is noteworthy that novel palladium complex **5c** displays a monomeric κ-acetato-ligand.[16]

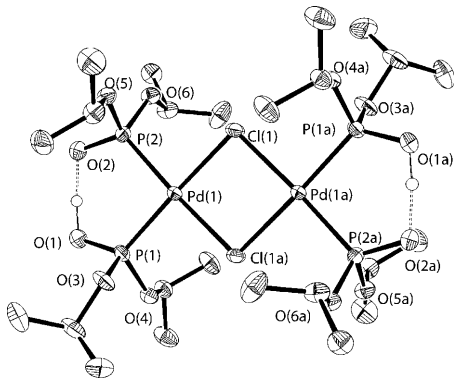
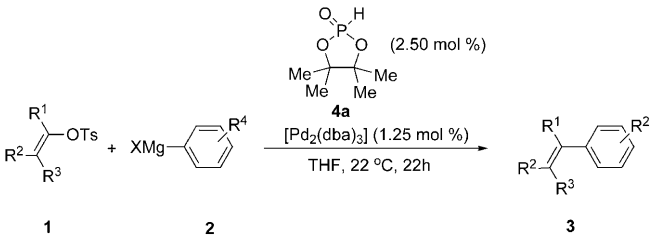


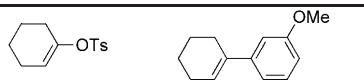
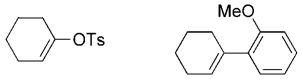
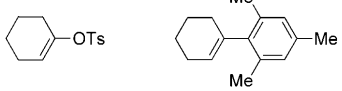
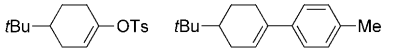
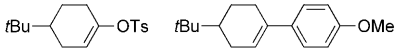
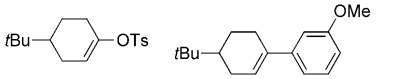
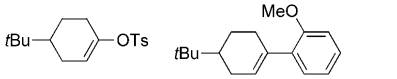
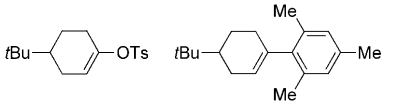
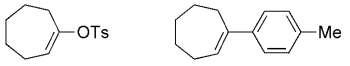
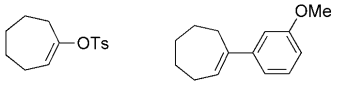
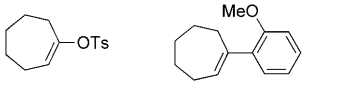
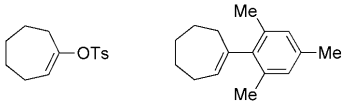
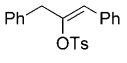
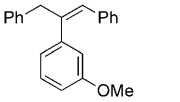
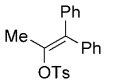
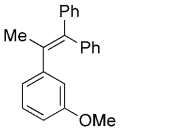
Figure 1. Molecular structure of $[(\mu\text{-ClPd}\{(i\text{PrO})_2\text{POH}\}\{(i\text{PrO})_2\text{PO}\})_2]$ (**5b**). Thermal ellipsoids are shown at 50% probability. H atoms are omitted for clarity except for H1O, which was found and refined freely.

Well-defined isolated catalysts for cross-couplings with aryl tosylates: With well-defined palladium complexes **5a**–**5c** in hand, we tested their catalytic efficacy in the Kumada–Corriu cross-coupling of electron-rich aryl tosylates **1a** and **1b** (Scheme 3). Notably, the isolated complex **5a** displayed an activity that was significantly improved over the one of the in situ generated catalytic system. Furthermore, palladium complexes **5b** and **5c** required a higher catalyst loading to ensure satisfactory yields of products **3ao** and **3ap**.

Subsequently, we explored the scope of the optimal catalyst **5a** in Kumada–Corriu cross-coupling reactions of substituted aryl tosylates (Table 2). Thus, diversely decorated aryl tosylates were efficiently functionalized, even when being

Table 1. Kumada–Corriu cross-coupling of alkenyl tosylates **1** with an in situ generated complex of HASPO **4a**.[a]



Entry	1	3		Yield [%]
1			**3aa**	65
2			**3ab**	77[b]
3			**3ac**	78[b]
4			**3ad**	72
5			**3ae**	73
6			**3af**	72
7			**3ag**	80[b]
8			**3ah**	82[b]
9			**3ai**	65
10			**3aj**	82
11			**3ak**	62[b]
12			**3al**	78[b]
13			**3am**	54
14			**3an**	70

[a] Reaction conditions: **1** (1.0 equiv), **2** (1.5 equiv), $[Pd_2(dba)_3]$ (1.25 mol %), **4a** (2.50 mol %), THF (2.0 mL), 22 h, 22 °C. [b] 60 °C.

electron-rich, hence for an oxidative addition electronically deactivated. Interestingly, the general synthesis of more sterically congested *ortho*-substituted biaryls proved also viable at a low catalyst loading.

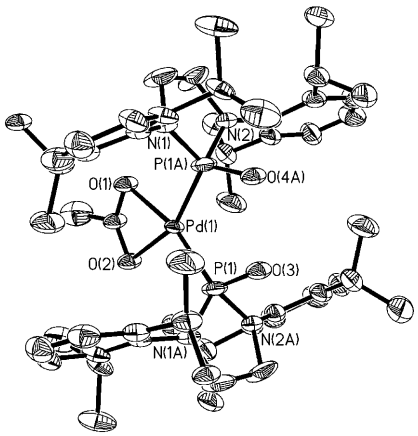
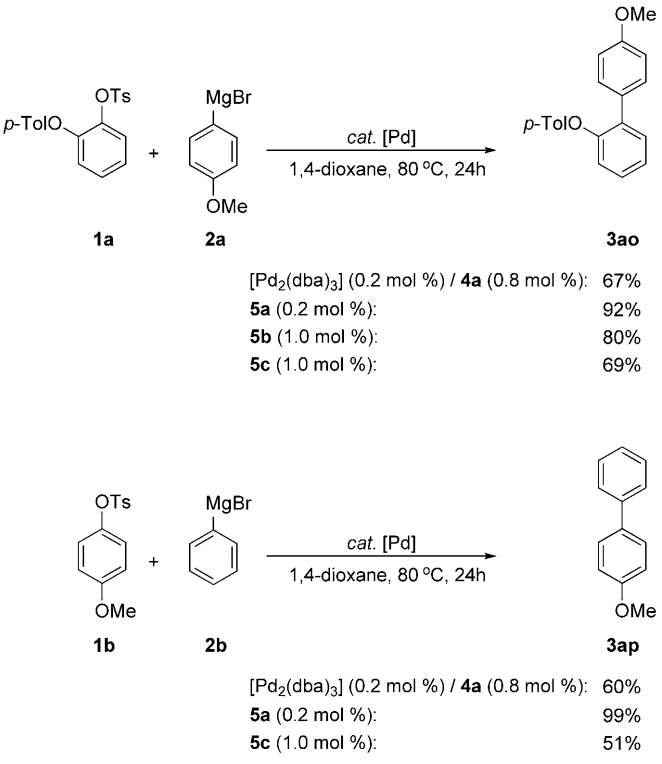


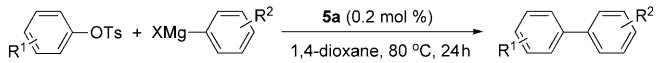
Figure 2. Molecular structure of κ^2-acetato palladium complex **5c**. Thermal ellipsoids are shown at 50 % probability. H atoms and solvent are omitted for clarity. Only one of two orientations of the disordered molecule is shown.



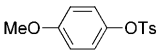
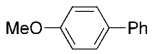
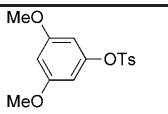
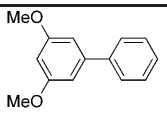
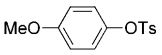
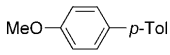
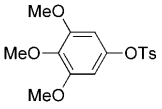
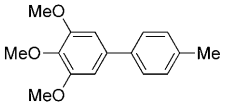
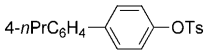
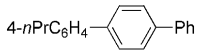
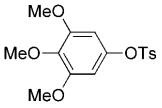
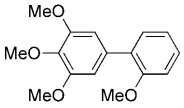
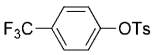
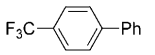
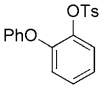
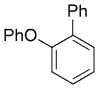
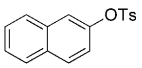
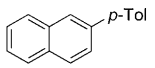
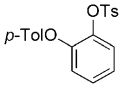
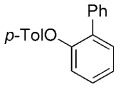
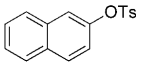
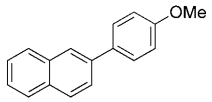
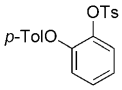
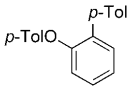
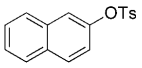
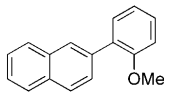
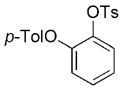
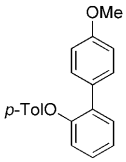
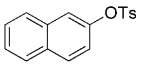
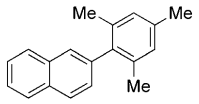
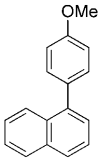
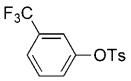
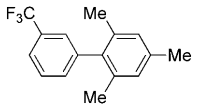
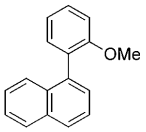
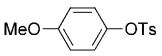
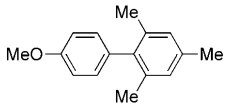
Scheme 3. Catalytic activity of isolated complexes **5** versus in situ generated catalyst.

Cross-couplings of N-heteroaryl tosylates: Regioselectively substituted N-heteroarenes are omnipresent structural motifs of biologically active compounds, and their syntheses by cross-coupling chemistry have received increased attention in recent years.[17] We, therefore, tested the use of air-stable complex **5a** in the Kumada–Corriu cross-coupling of nitrogen-containing heterocyclic tosylates. Contrary to the results obtained with a previously reported palladium cata-

Table 2. Scope of Kumada-Corriu cross-coupling of aryl tosylates **1** with catalyst **5a**.[a]



1 **2** **3**

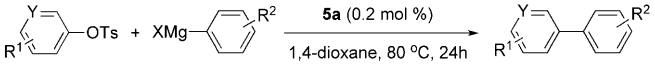
Entry	1	3		Yield [%]	Entry	1	3		Yield [%]
1			**3ap**	99	12			**3ba**	94
2			**3aq**	89	13			**3bb**	97
3			**3ar**	94	14			**3bc**	98
4			**3as**	74	15			**3bd**	74
5			**3at**	91	16			**3be**	79
6			**3au**	98	17			**3bf**	94
7			**3av**	97	18			**3ao**	92 94[c]
8			**3aw**	83[b]	19			**3bg**	84
9			**3ax**	71[b]	20			**3bh**	94 88[c]
10			**3ay**	71[b]	21			**3bi**	97
11			**3az**	84	22			**3bj**	93

[a] Reaction conditions: **1** (1.0 equiv), **2** (1.5 equiv), **5a** (0.2 mol %) 1,4-dioxane (4.0 mL), 24 h, 80 °C. [b] **5c** (2.0 mol %), 110 °C. [c] **5c** (2.0 mol %), 22 °C.

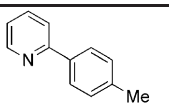
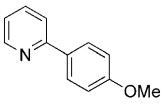
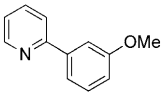
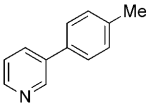
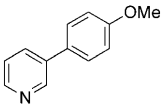
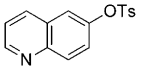
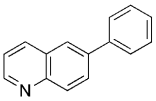
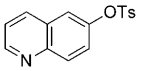
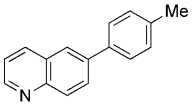
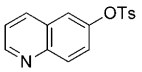
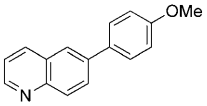
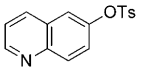
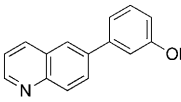
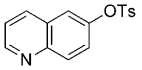
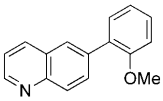
lyst,[8] excellent yields were generally obtained with HASPO-derived catalyst **5a** (Table 3), thereby furnishing regioselectively decorated pyridines (Table 3, entries 1–5) and quinolines (Table 3, entries 6–10), again at remarkably low catalyst loading.

Alkenyl tosylates: Alkenyl tosylates are useful, yet challenging starting materials for the diastereoselective synthesis of substituted alkenes. Hence, we were delighted to observe that the well-defined palladium complex **5a** also allowed highly efficient cross-coupling reactions of electronically un-

Table 3. Kumada–Corriu cross-coupling of heteroaryl tosylates **1** with isolated complex **5a**.[a]



1 **2** **3**

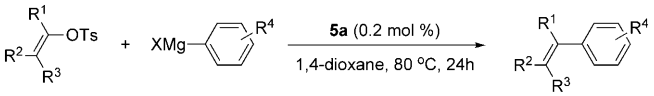
Entry	**1**	**3**		Yield [%]
1			**3bk**	83
2			**3bl**	98
3			**3bm**	92
4			**3bn**	71
5			**3bo**	72
6			**3bp**	91
7			**3bq**	92
8			**3br**	94
9			**3bs**	98
10			**3bt**	97

[a] Reaction conditions: **1** (1.0 equiv), **2** (1.5 equiv), **5a** (0.2 mol %), 1,4-dioxane (4.0 mL), 24 h, 80 °C.

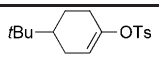
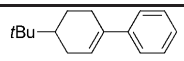
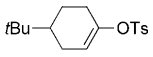
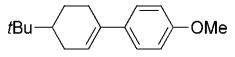
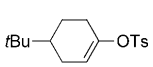
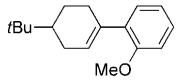
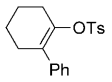
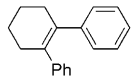
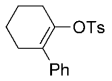
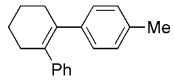
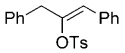
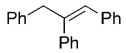
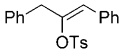
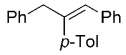
activated alkenyl tosylates **1** (Table 4). Notably these transformations proceeded with excellent stereocontrol, thereby delivering the desired alkenes **3** as the sole products.

Hydroxyl-substituted electrophiles: Subsequently, we were interested in the site-selective cross-coupling of dihalo-substituted arenes.[18–20] Consequently, we explored the use of air-stable complex **5a** for the functionalization of electrophiles **1** bearing free acidic hydroxyl substituents[19,21–23] as potential directing groups (Table 5). Notably, both aryl chlorides as well as aryl tosylates displaying free hydroxyl groups were converted to the desired products **3** with high chemoselectivities (Table 5, entries 1–5). Moreover, benzyl

Table 4. Kumada–Corriu cross-coupling of alkenyl tosylates **1** with complex **5a**.[a]



1 **2** **3**

Entry	**1**	**3**		Yield [%]
1			**3bu**	83
2			**3ae**	92
3			**3ag**	62
4			**3bv**	90
5			**3bw**	94
6			**3bx**	96
7			**3by**	98
8			**3bz**	97
9			**3ca**	97

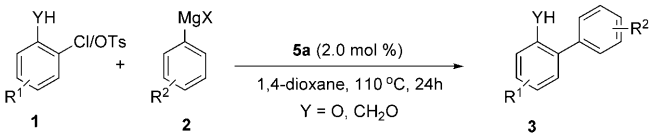
[a] Reaction conditions: **1** (1.0 equiv), **2** (1.5 equiv), **5a** (0.2 mol %), 1,4-dioxane (4.0 mL), 24 h, 80 °C.

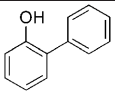
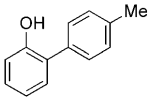
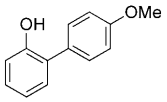
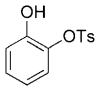
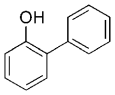
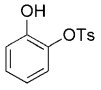
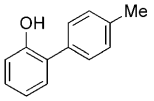
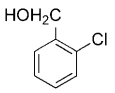
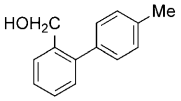
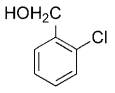
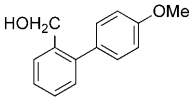
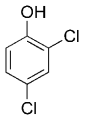
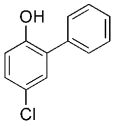
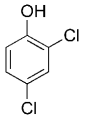
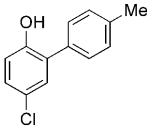
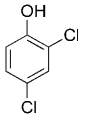
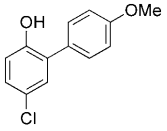
alcohols **1** were well tolerated by homobimetallic complex **5a** as well (Table 5, entries 6 and 7). Importantly, these findings finally set the stage for site-selective Kumada–Corriu cross-couplings of dichloroarenes (Table 5, entries 8–10).

Conclusion

In summary, we have reported on the synthesis of novel well-defined palladium complexes derived from HASPO preligands, which were fully characterized, including their X-ray crystal structure analysis. Importantly, an air-stable complex of PinP(O)H (**4a**) displayed a significantly improved catalytic activity in the challenging cross-coupling of unactivated aryl tolsylates, when compared with the in situ generated catalytic system. The optimized catalysts remarkably broad substrate scope was reflected by high-yielding cross-couplings of alkenyl and heteroaryl tosylates at low catalyst loadings, as well as chemo- and site-selective functionalizations of hydroxyl-substituted electrophiles. More generally, the unprecedented use of isolated HASPO complexes for cross-coupling reactions has shed light on the working mode of thus far in situ generated HASPO-based catalytic systems.

Table 5. Kumada–Corriu cross-coupling of hydroxyl-substituted electrophiles **1**.[a]



Entry	1	3		Yield [%]
1			**3cb**	75
2			**3cc**	73
3			**3cd**	82
4			**3cb**	84
5			**3cc**	80
6			**3ce**	77
7			**3cf**	93
8			**3cg**	86
9			**3ch**	73
10			**3ci**	75

[a] Reaction conditions: **1** (1.0 equiv), **2** (3.0 equiv), **5a** (2.0 mol %), 1,4-dioxane (4.0 mL), 24 h, 110 °C.

Experimental Section

General remarks: Catalytic reactions were carried out under a N_2 atmosphere using pre-dried glassware. Chemicals were obtained from commercial sources, and were used without further purification. Aryl[14] and alkenyl[24] tosylates were prepared as previously described. 1,4-Dioxane and THF were freshly distilled from sodium/benzophenone under N_2. Yields refer to isolated compounds, estimated to be >95% pure as determined by ^{1}H NMR and GC analysis. Flash chromatography: Macherey–Nagel silica gel 60 (70–230 mesh). NMR: Spectra were recorded on a Varian-NMR 300 instrument in the solvent indicated; chemical shifts (δ) are given in ppm.

Representative procedure for Kumada–Corriu cross-coupling reactions of alkenyl tosylates 1 with the in situ generated catalyst: Synthesis of 3ae (Table 1, entry 5): A solution of $[Pd_2(dba)_3]$ (5.80 mg, 0.006 mmol, 1.2 mol %) and PinP(O)H (**4a**) (2.10 mg, 0.013 mmol, 2.5 mol %) in dry THF (2.00 mL) was stirred under N_2 for 5 min at ambient temperature. Then **2a** (1.50 mL, 0.5 M in THF, 0.75 mmol) was added by using a syringe and the solution was stirred for an additional 5 min at ambient temperature. Thereafter, 4-*tert*-butylcyclohexen-1-yltosylate (160 mg, 0.519 mmol) was added, and the resulting suspension was stirred for 22 h at ambient temperature. Saturated, aqueous NH_4Cl solution (50 mL) and EtOAc (50 mL) were added, and the separated aqueous phase was extracted with EtOAc (3×50 mL). The combined organic layers were concentrated in vacuo and the remaining residue was purified by column chromatography on silica gel (*n*-pentane) to yield **3ae** (90 mg, 73 %) as a colorless solid (m.p. 77–78 °C).

Representative procedure for the palladium-catalyzed Kumada–Corriu cross-coupling reactions of aryl tosylates with palladium complex 5a: Synthesis of 3ap (Scheme 3): A solution of **5a** (1.8 mg, 0.002 mmol, 0.2 mol %) in dry 1,4-dioxane (4.00 mL) was stirred under N_2 for 5 min at ambient temperature. Then **2b** (0.68 mL, 2.2 M in THF, 1.50 mmol) was added by using a syringe and the solution was stirred for an additional 5 min. Thereafter **1b** (278 mg, 1.00 mmol) was added, and the resulting suspension was stirred for 24 h at 80 °C. At ambient temperature, aqueous HCl (2.0 mL, 2.0 M), EtOAc (10 mL), and H_2O (10 mL) were added, and the separated aqueous phase was extracted with EtOAc (2×20 mL). The combined organic layers were concentrated in vacuo and the remaining residue was purified by column chromatography (*n*-hexane/EtOAc: 200/1) to yield **3ap** (182 mg, 99 %) as a colorless solid (m.p. 88–89 °C).

Acknowledgements

Generous support by the DFG and the Alexander-von-Humboldt foundation (fellowship to A.K.), and the State of Lower Saxony within the CaSUS program (fellowship to C.K.) is gratefully acknowledged.

[1] L. Ackermann, *Modern Arylation Methods*, Wiley-VCH, Weinheim, **2009**.
[2] M. Beller, C. Bolm, *Transition Metals for Organic Synthesis*, 2nd ed., Wiley-VCH, Weinheim, **2004**.
[3] A. F. Littke in *Modern Arylation Methods* (Ed.: L. Ackermann), Wiley-VCH, Weinheim, **2009**, pp. 25–68.
[4] A. F. Littke, G. C. Fu, *Angew. Chem.* **2002**, *114*, 4350–4386; *Angew. Chem. Int. Ed.* **2002**, *41*, 4176–4211.
[5] J. Tsuji, *Palladium Reagents and Catalysts*, 2nd ed., Wiley, New York, **2004**.
[6] For representative examples of arylations with challenging aryl sulfonates, see: a) M. L. H. Mantel, A. T. Lindhardt, D. Lupp, T. Skrydstrup, *Chem. Eur. J.* **2010**, *16*, 5437–5442; b) D. A. Wilson, C. J. Wilson, C. Moldoveanu, A.-M. Resmerita, P. Corcoran, L. M. Hoang, B. M. Rosen, V. Percec, *J. Am. Chem. Soc.* **2010**, *132*, 1800–1801; c) W. K. Chow, C. M. So, C. P. Lau, F. Y. Kwong, *J. Org. Chem.* **2010**, *75*, 5109–5112; d) L. Ackermann, A. Althammer, S. Fenner, *Angew. Chem.* **2009**, *121*, 207–210; *Angew. Chem. Int. Ed.* **2009**, *48*, 201–204; e) C. M. So, C. P. Lau, F. Y. Kwong, *Angew. Chem.* **2008**, *120*, 8179–8183; *Angew. Chem. Int. Ed.* **2008**, *47*, 8059–8063; f) L. Zhang, J. Wu, *Adv. Synth. Catal.* **2008**, *350*, 2409–2413; g) C. M. So, Z. Zhou, C. P. Lau, F. Y. Kwong, *Angew. Chem.* **2008**, *120*, 6502–6506; *Angew. Chem. Int. Ed.* **2008**, *47*, 6402–6406; h) L. Ackermann, M. Mulzer, *Org. Lett.* **2008**, *10*, 5043–5045; i) L. Zhang, J. Wu, *J. Am. Chem. Soc.* **2008**, *130*, 12250–12251; j) A. L. Hansen, J.-P. Ebran, M. Ahlquist, P.-O. Norrby, T. Skrydstrup, *Angew. Chem.* **2006**, *118*, 3427–3431; *Angew. Chem. Int. Ed.* **2006**, *45*, 3349–3353; k) L. Ackermann, A. Althammer, R. Born, *Angew. Chem.* **2006**, *118*, 2681–2685; *Angew. Chem. Int. Ed.* **2006**, *45*, 2619–2622; l) H. N. Nguyen, X. Huang, S. L. Buchwald, *J. Am. Chem. Soc.* **2003**,

125, 11818–11819; m) D. Gelman, S. L. Buchwald, *Angew. Chem.* **2003**, *115*, 6175–6178; *Angew. Chem. Int. Ed.* **2003**, *42*, 5993–5996; and references therein.

[7] A. H. Roy, J. F. Hartwig, *J. Am. Chem. Soc.* **2003**, *125*, 8704–8705.

[8] M. E. Limmert, A. H. Roy, J. F. Hartwig, *J. Org. Chem.* **2005**, *70*, 9364–9370.

[9] For an early example of Kumada–Corriu cross-coupling reactions with aryl tosylates using transition metals other than palladium, see: a) E. Wenkert, E. L. Michelotti, C. S. Swindell, M. Tingoli, *J. Org. Chem.* **1984**, *49*, 4894–4899; through aryne formation: b) C.-G. Dong, Q.-S. Hu, *Org. Lett.* **2006**, *8*, 5057–5060.

[10] Representative reviews on direct functionalizations of heteroarenes, for which achieving regioselectivity continues to be challenging: a) L. Ackermann, *Chem. Commun.* **2010**, *46*, 4866–4877; b) L. Joucla, L. Djakovitch, *Adv. Synth. Catal.* **2009**, *351*, 673–714; c) F. Bellina, R. Rossi, *Tetrahedron* **2009**, *65*, 10269–10310; d) L. Ackermann, R. Vicente, A. Kapdi, *Angew. Chem.* **2009**, *121*, 9976–10011; *Angew. Chem. Int. Ed.* **2009**, *48*, 9792–9826; e) I. V. Seregin, V. Gevorgyan, *Chem. Soc. Rev.* **2007**, *36*, 1173–1193, and references therein.

[11] For reviews on secondary phosphine oxide (SPO) preligands: a) L. Ackermann, *Synthesis* **2006**, 1557–1571; b) L. Ackermann in *Trivalent Phosphorus Compounds in Asymmetric Catalysis: Synthesis and Applications* (Ed.: A. Börner), Wiley-VCH, Weinheim, **2008**, 831–847; c) N. V. Dubrovina, A. Börner, *Angew. Chem.* **2004**, *116*, 6007–6010; *Angew. Chem. Int. Ed.* **2004**, *43*, 5883–5886; for recent representative examples of SPO preligands in cross-coupling reactions, see: d) L. Ackermann, A. R. Kapdi, C. Schulzke, *Org. Lett.* **2010**, *12*, 2298–2301; e) L. Ackermann, R. Vicente, N. Hofmann, *Org. Lett.* **2009**, *11*, 4274–4276; f) D. X. Yang, S. L. Colletti, K. Wu, M. Song, G. Y. Li, H. C. Shen, *Org. Lett.* **2009**, *11*, 381–384; g) H. Xu, K. Ekoue-Kovi, C. Wolf, *J. Org. Chem.* **2008**, *73*, 7638–7650; h) L. Ackermann, R. Vicente, A. Althammer, *Org. Lett.* **2008**, *10*, 2299–2302; i) C. Wolf, H. Xu, *J. Org. Chem.* **2008**, *73*, 162–167; j) Z. Zhang, Z. Hu, Z. Yu, P. Lei, H. Chi, Y. Wang, R. He, *Tetrahedron Lett.* **2007**, *48*, 2415–2419; k) R. Lerebours, C. Wolf, *Org. Lett.* **2007**, *9*, 2737–2740; l) L. Ackermann, R. Born, P. Álvarez-Bercedo, *Angew. Chem.* **2007**, *119*, 6482–6485; *Angew. Chem. Int. Ed.* **2007**, *46*, 6364–6367; m) R. Lerebours, C. Wolf, *J. Am. Chem. Soc.* **2006**, *128*, 13052–13053; n) R. Lerebours, A. Camacho-Soto, C. Wolf, *J. Org. Chem.* **2005**, *70*, 8601–8604; o) C. Wolf, R. Lerebours, *Org. Lett.* **2004**, *6*, 1147–1150; p) G. Y. Li, *J. Org. Chem.* **2002**, *67*, 3643–3650; q) G. Y. Li, *Angew. Chem.* **2001**, *113*, 1561–1564; *Angew. Chem. Int. Ed.* **2001**, *40*, 1513–1516; for recent studies on the coordination chemistry of SPOs, see: r) T. Achard, L. Giordano, A. Tenaglia, Y. Gimbert, G. Buono, *Organometallics* **2010**, *29*, 3936–3950; s) A. Christiansen, D. Selent, A. Spannenberg, W. Baumann, R. Franke, A. Börner, *Organometallics* **2010**, *29*, 3139–3145; t) A. Christiansen, C. Li, M. Garland, D. Selent, R. Ludwig, A. Spannenberg, W. Baumann, R. Franke, A. Börner, *Eur. J. Org. Chem.* **2010**, 2733–2741, and references therein.

[12] For reviews, see: a) L. Ackermann, *Pure Appl. Chem.* **2010**, *82*, 1403–1413; b) L. Ackermann, A. Althammer, *Chem. Unserer Zeit* **2009**, *43*, 74–83; c) L. Ackermann, *Synlett* **2007**, 507–526; d) T. Nemoto, Y. Hamada, *Chem. Rec.* **2007**, *7*, 150–158; e) L. Ackermann, R. Born, J. H. Spatz, A. Althammer, C. J. Gschrei, *Pure Appl. Chem.* **2006**, *78*, 209–214.

[13] For select examples, see: a) L. Ackermann, H. K. Potukuchi, A. Althammer, R. Born, P. Mayer, *Org. Lett.* **2010**, *12*, 1004–1007; b) L. Ackermann, C. Wechsler, A. R. Kapdi, A. Althammer, *Synlett* **2010**, 294–298; c) L. Ackermann, H. K. Potukuchi, *Synlett* **2009**, 2852–2856; d) L. Ackermann, S. Barfüßer, *Synlett* **2009**, 808–812; e) I. Pryjomska, H. Bartosz-Bechowski, Z. Ciunik, A. M. Trzeciak, J. J. Ziolkowski, *Dalton Trans.* **2006**, 213–220; f) L. Ackermann, J. H. Spatz, C. J. Gschrei, R. Born, A. Althammer, *Angew. Chem.* **2006**, *118*, 7789–7792; *Angew. Chem. Int. Ed.* **2006**, *45*, 7627–7630; g) L. Ackermann, C. J. Gschrei, A. Althammer, M. Riederer, *Chem. Commun.* **2006**, 1419–1421; h) L. Ackermann, R. Born, J. H. Spatz, D. Meyer, *Angew. Chem.* **2005**, *117*, 7382–7386; *Angew. Chem. Int. Ed.* **2005**, *44*, 7216–7219; i) L. Ackermann, R. Born, *Angew. Chem.* **2005**, *117*, 2497–2500; *Angew. Chem. Int. Ed.* **2005**, *44*, 2444–2447.

[14] L. Ackermann, A. Althammer, *Org. Lett.* **2006**, *8*, 3457–3460.

[15] CCDC-771116 (**5a**), CCDC-788126 (**5b**) and CCDC-771115 (**5c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[16] For a platinum complex bearing phosphinous acid ligands, see: a) J. Bigeault, L. Giordano, I. De Riggi, Y. Gimbert, G. Buono, *Org. Lett.* **2007**, *9*, 3567–3570; b) a phosphinous acid palladium complex: L. Ackermann, H. K. Potukuchi, A. R. Kapdi, C. Schulzke, *Chem. Eur. J.* **2010**, *16*, 3300–3303.

[17] Select reviews: a) C. Torborg, M. Beller, *Adv. Synth. Catal.* **2009**, *351*, 3027–3043; b) I. J. S. Fairlamb, *Chem. Soc. Rev.* **2007**, *36*, 1036–1045; c) G. Zeni, R. C. Larock, *Chem. Rev.* **2006**, *106*, 4644–4680; d) M. Schnürch, R. Flasik, A. F. Khan, M. Spina, M. D. Mihovilovic, P. Stanetty, *Eur. J. Org. Chem.* **2006**, 3283–3307; e) K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem.* **2005**, *117*, 4516–4563; *Angew. Chem. Int. Ed.* **2005**, *44*, 4442–4489, and references therein.

[18] S. Schröter, C. Stock, T. Bach, *Tetrahedron* **2005**, *61*, 2245–2267.

[19] J.-R. Wang, K. Manabe, *Synthesis* **2009**, 1405–1427.

[20] For representative examples of site-selective cross-couplings of di- or oligohalo-substituted arenes, see: a) S. A. Schweizer, T. Bach, *Synlett* **2010**, 81–84; b) M. Hussain, T. H. Nguyen, R. A. Khera, I. Malik, D. S. Zinad, P. Langer, *Adv. Synth. Catal.* **2010**, *352*, 1429–1433; c) L. Ackermann, A. Althammer, P. Mayer, *Synthesis* **2009**, 3493–3503; d) I. N. Houpis, J-C. P. Hoeck, U. Tilstam, *Synlett* **2007**, 2179–2184; e) L. Ackermann, A. Althammer, *Angew. Chem.* **2007**, *119*, 1652–1654; *Angew. Chem. Int. Ed.* **2007**, *46*, 1627–1629; f) T. Schaub, M. Backes, U. Radius, *J. Am. Chem. Soc.* **2006**, *128*, 15964–15965; g) L. T. Kaspar, L. Ackermann, *Tetrahedron* **2005**, *61*, 11311–11316; h) L. Ackermann, *Org. Lett.* **2005**, *7*, 439–442; i) F. Kakiuchi, M. Usui, S. Ueno, N. Chatani, S. Murai, *J. Am. Chem. Soc.* **2004**, *126*, 2706–2707; j) S. M. Dirk, D. W. Price, S. Chanteau, D. V. Kosynkin, J. M. Tour, *Tetrahedron* **2001**, *57*, 5109–5121; k) F. Bellina, C. Anselmi, S. Viel, L. Mannina, R. Rossi, *Tetrahedron* **2001**, *57*, 9997–10007; l) Y. Ishii, N. Chatani, S. Yorimitsu, S. Murai, *Chem. Lett.* **1998**, 157–158; m) R. Singh, G. Just, *J. Org. Chem.* **1989**, *54*, 4453–4457; n) A. Minato, K. Suzuki, K. Tamao, *J. Am. Chem. Soc.* **1987**, *109*, 1257–1258, and references therein.

[21] S. Ishikawa, K. Manabe, *Angew. Chem.* **2010**, *122*, 784–787; *Angew. Chem. Int. Ed.* **2010**, *49*, 772–775.

[22] S. Ishikawa, K. Manabe, *Chem. Lett.* **2007**, *36*, 1304–1305.

[23] S. Ishikawa, K. Manabe, *Org. Lett.* **2007**, *9*, 5593–5595.

[24] A. Klapars, K. R. Campos, C.-y. Chen, R. P. Volante, *Org. Lett.* **2005**, *7*, 1185–1188.

Received: August 18, 2010
Published online: February 3, 2011

