Selective Monoarylation of Primary Anilines Catalyzed by Pd(dippf) and its Application in OLED Component Synthesis

Matthias F. Grünberg,^a Fan Jia,^a Andreas Rivas-Nass,^b and Lukas J. Gooßen^{a,*}

^a Department of Chemistry, University of Kaiserslautern, Erwin-Schrödinger-Strasse 54, 67663 Kaiserslautern, Germany Fax: (+49)-631-205-3921; phone: (+49)-631-205-2046; e-mail: goossen@chemie.uni-kl.de

^b Precious Metals Chemistry, Umicore AG & Co. KG, Rodenbacher Chaussee 4, 63457 Hanau-Wolfgang, Germany

Received: December 22, 2015; Revised: March 3, 2016; Published online: May 3, 2016

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201501160.

Abstract: Palladium 1,1'-bis(diisopropylphosphino)ferrocene [Pd(dippf)] complexes were found to promote the monoarylation of primary anilines with unprecedented selectivities. They also allow the sequential arylation of primary anilines with two different aryl bromides in one pot. The reactions can be performed at low catalyst loadings (0.2 mol%) and high substrate concentrations. The synthetic utility of the optimum catalyst was demonstrated by the synthesis of various di- and triarylamines. A particular focus was set on compounds with carbazole and fluorene moieties as employed in state-ofthe-art small-molecule organic light emitting diodes (OLEDs).

Keywords: amination; homogeneous catalysis; OLEDs; organic light emitting diodes; palladium; phosphine ligands

Within recent years, organic light emitting diode (OLED) technology has undergone significant development.^[1] Since the first report by Tang and Van Slyke in 1987,^[2] tremendous research efforts have vastly improved the performance and lifetime of electroluminescent materials. This has enabled their broad application in digital displays and solid-state lighting.^[3] Both polymer-based devices^[4] and smallmolecule OLEDs are highly efficient and durable.^[1c] The advantage of the latter is that their molecular design may be altered with great flexibility, and the components can conveniently be deposited in precise thin layers by vacuum sublimation techniques.^[5]

Such small-molecule OLEDs have multilayered structures in which emitter layers are positioned between electron- and hole-transporting layers and the electrode materials. The hole transport materials often contain triarylamines with carbazole^[6] and fluo-



Figure 1. Modern hole transport materials.^[6f]

rene^[7] substructures (Figure 1), since these have high thermal stabilities ($\Delta T_{5\%}$) and high glass transition temperatures (T_g). However, these important parameters strongly depend on the purity of the materials, and longevity of the electronic devices at top performance can only be assured if their chemical synthesis proceeds with excellent selectivity. Thus, efficient syntheses of triarylamines are constantly sought.

The Buchwald–Hartwig amination, a palladiummediated arylation of amines with aryl halides, is arguably the most versatile and efficient synthetic entry to this important substrate class (Scheme 1).^[8,9] However, the arylation of fluorenylamines with bulky aryl bromides proceeds rather sluggishly even with stateof-the-art catalysts. Usually, high loadings in excess of



Scheme 1. Traditional and targeted triarylamine syntheses.



Figure 2. Selection of investigated ligands.

1% catalyst are required, and significant quantities of hard-to-separate diarylation products are produced, so that isolation and purification of the diarylamine intermediates is indispensable.

The key towards enabling a straightforward, onepot synthesis of small-molecule OLEDs lies in the development of a highly selective and easily scalable monoarylation protocol that would proceed at high substrate concentrations and low catalyst loadings with only equimolar amounts of the coupling partners.

In search of an efficient catalyst system, we investigated various state-of-the-art amination ligands for Pd (Figure 2) using the model reaction of aniline (**1a**) with 4-bromotoluene (**2a**), with NaO-*t*-Bu as the base and toluene as the solvent.^[8] Table 1 shows that most of the Pd/phosphine catalysts led to full conversion of the starting materials within 20 h at 70 °C (entries 1– 8). Interestingly, the reaction proceeded more slowly with Pd-NHC catalysts, resulting in low yields (entries 9 and 10).

However, the formation of the desired diarylamine 3a was always accompanied by the formation of 1-4% of the diarylated by-product 5a, which could be easily detected by GC.^[10] Surprisingly, we found that diarylation can completely be suppressed with 1,1'bis(diisopropylphosphino)ferrocene (dippf), a ligand that has only rarely been employed in cross-coupling reactions (entry 13).^[11] However, further experiments confirmed its unique selectivity among aryl- or alkylsubstituted ferrocenyl phosphines (entries 11–13). Pd(dippf) catalysts generated *in situ* from the Pd(0)precursors $Pd(dba)_2$ or Pd(vs) (vs = 1,3-divinyl-1,1,3,3tetramethyldisiloxane) proved to be most active, while in situ generated Pd(dippf)Cl₂ showed almost no activity (entry 14). In the presence of Pd(dippf) catalysts, product 5a was not even detected in traces.

Adding a dippf solution in toluene to Pd(vs) (10.87% Pd) results in a stable catalyst solution that can be stored and handled easily. Alternatively, Pd(dippf) can be precipitated as a defined maleimide

 Table 1. Benchmarking of state-of-the-art amination catalysts.^[a]

	, n Tol Br	Pd-source (0.2 mol%) ligand (0.2 mol%) NaO- <i>t</i> -Bu (1.2 equiv.)	p-Tol │	p-Tol
Pn-NH ₂ ·	+ <i>μ</i> -τοι-Βι	toluene	Ph ^N H	⁺ Ph ^N Tol-p
1a	2a	70 °C, 20 h	3a	5a

Entry	Pd source	Ligand	Yield [%]	
-		-	3 a	5a
1	$Pd[P(t-Bu)_3]_2$	_	91	4
2	$\{Pd(\mu Br)[P(t-Bu)_3]\}_2$	_	90	4
3	$Pd(dba)_2$	JohnPhos	90	2
4	$Pd(dba)_2$	XPhos	94	4
5	$Pd(dba)_2$	BrettPhos	87	1
6	$Pd(dba)_2$	BINAP	71	1
7	$Pd(dba)_2$	XantPhos	88	2
8	$Pd(dba)_2$	dppf	72	1
9	(IPr)Pd(allyl)Cl	_	9	n.d.
10	(IPr)Pd(cinnamyl)Cl	_	7	n.d.
11	$Pd(dba)_2$	dcypf	76	trace
12	$Pd(dba)_2$	dtbupf	92	3
13	$Pd(dba)_2$	dippf	94	n.d.
14	PdCl ₂	dippf	5	n.d.
15	Pd(dippf)vs	_	92	n.d.
16	Pd(dippf)maleimide	dippf	93	n.d.

[a] Conditions: 1.00 mmol of 1a, 1.00 mmol of 2a, 1.20 mmol NaO-t-Bu, 0.2 mol% Pd source, 0.3 mol% of a monodentate ligand or 0.2 mol% of a bidentate ligand, 1 mL of toluene, 70°C, 20 h. GC yields with *n*-tetradecane as internal standard; n.d.=not detected, vs=1,3-divinyl-1,1,3,3-tetramethyldisiloxane.



Scheme 2. Pd(dippf)maleimide (6) synthesis.

adduct from a mixture of maleimide and Pd(dippf)vs in diethyl ether (Scheme 2). Pd(dippf)maleimide (6) is an air-stable, yellow solid with slightly lower reactivity than the catalysts generated *in situ*. However, in combination with additional dippf, it is superior to the catalysts generated *in situ* with regard to activity and long-term stability, especially at elevated temperatures (entry 16, see also the Supporting Information).



Figure 3. ORTEP drawing of Pd(dippf)maleimide **6** (50% probability ellipsoids).

The structure of complex **6** features a dippf bite angle of 105.9° and an η^2 -coordinated maleimide ligand (Figure 3).^[12]

After the encouraging findings with the simple test system, we probed the activity of various catalysts in the synthesis of large conjugated π -systems as used in OLEDs (Scheme 3).^[13] Because even trace impurities may strongly affect the conductivity of these electrical materials or lead to their premature deterioration resulting in so-called "black spots",^[14] an unusually high level of selectivity needed to be ensured in this reaction.

Simple TLC analysis proved to be most sensitive in the detection of diarylated by-products because of their extreme absorption under UV light.

In the arylation of **1b** with **2b**, the dippf catalysts led to full conversion within 16 h at 70 °C. The undesired diarylation product was not detected even in traces by TLC. Against a benchmark of Pd catalysts



Scheme 3. Synthesis of π -conjugated amines.

© 2016 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

with $P(t-Bu)_3$ or Buchwald-type biarylphosphine ligands, the dippf systems were somewhat less reactive, but displayed unparalleled selectivity.^[13]

With the optimal catalyst system in hand, we examined the scope of the monoarylation (Table 2). Several mono- and polycyclic aromatic amines, as well as amines with dibenzofuran, dibenzothiophene, pyridine, carbazole, and fluorene residues were converted to the corresponding secondary amines in excellent yields and selectivities. Many of these structures are currently under investigations for use in OLEDs. In the presence of the strong base NaO-t-Bu, only robust functionalities such as chlorine, methyl sulfide, and methoxy remain unchanged. However, when switching to cesium carbonate as the base, even sensitive functionalities such as ester, keto, and cyano groups are tolerated. The catalyst has only moderate reactivity because of its tremendous selectivity. In all cases, the selectivity for the monoarylated product is exceptionally high. The diarylation by-product is obtained in no case. It is even possible to perform monoarylations of primary anilines in the presence of secondary amine functionalities (Table 2, 3t).^[15]

The reaction was scaled up to a preparative scale. Thus, 7.97 g (20 mmol) of 3-(4-bromophenyl)-9-phenyl-9*H*-carbazole (**2b**) were converted to **3b** in 97% isolated yield in the presence of 0.2 mol% of **6**/ dippf.

We next investigated how the selective monoarylation of primary anilines can be combined with a second arylation into a one-pot synthesis of unsymmetrically substituted triarylamines. The arylation of aniline (1a) with 4-bromotoluene (2a), then with panisyl chloride (21) in the presence of NaO-t-Bu was used as a test reaction. The combination of 6 and dippf was again validated as a uniquely selective catalyst. Equimolar amounts of 1a and 2a were initially allowed to react for 20 h at 80 °C in the presence of 0.5 mol% catalyst, then 21 was added in a small excess, the temperature was increased to 120°C, and stirring was continued for another 24 h. In this way, the triarylamine 4a was obtained in high yield and selectivity. The same reaction protocol can also be applied to the coupling of the aniline 1a with two different aryl bromides. The advantage of using an aryl chloride as the second electrophile is its lower reactivity. As a result, 21 may also be added directly at the beginning without substantially impacting the selectivity.

Table 3 illustrates the scope of the one-pot unsymmetrical diarylation procedure. A particular focus was set on molecules with quinolinyl, quinazolyl and *N*-arylpyrrole moieties as used in contemporary hole transport materials within OLEDs. Aryl chlorides and bromides proved to be equally suited as coupling partners for the second step. All products were obtained in high yields and purities.





^[a] The residue originating from the aryl bromide is placed on the right-hand side. *Conditions:* 1.00 mmol of amine, 1.00 mmol of aryl bromide, 1.20 mmol of NaO-*t*-Bu, 0.2 mol% of **6**, 0.2 mol% of dippf, 2 mL of toluene, 70 °C, 20 h, isolated yields.

^[b] 1.20 mmol of Cs₂CO₃, 110 °C.

In conclusion, a catalyst system consisting of Pd(dippf)maleimide and dippf efficiently promotes the monoarylation of primary amines with unparalleled selectivity. At higher reaction temperatures, this catalyst also promotes a further arylation of the resulting diarylamines. This enables the one-pot, two-step synthesis of unsymmetrically substituted triarylamines in high yields and selectivities. This synthetic approach is effective in the synthesis of high-purity triarylamines with large conjugated π -systems as used in modern OLEDs as hole transport materials.

Experimental Section

Standard Procedure for the Selective Monoarylation of Primary Amines

A dry 20-mL crimp-cap vessel was charged with the aryl bromide (1.00 mmol), the primary amine (1.00 mmol), sodium *tert*-butoxide (118 mg, 1.20 mmol) and a magnetic stir bar and was kept in vacuum for 10 min. After three ni-

trogen-vacuum cycles, a stock solution of Pd(dippf)maleimide (1.24 mg, 0.002 mmol) and dippf (0.85 mg, 0.002 mmol) in dry, distilled toluene (2 mL) was added *via* syringe. The reaction mixture was stirred at 70 °C for 20 h, cooled to room temperature and diluted with dichloromethane (30 mL) and water (30 mL). The aqueous layer was separated and extracted with dichloromethane (2×20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum (40 °C, 500 mbar). The crude product was further purified by flash chromatography (SiO₂ or basic Al₂O₃, hexane/ethyl acetate or hexane/ diethyl ether), yielding the corresponding amine; yield: 70– 96%.

One-Pot Procedure for the Synthesis of Tertiary Amines

A dry 20-mL crimp-cap vessel was charged with the aryl bromide (1.00 mmol), the primary amine (1.00 mmol), sodium *tert*-butoxide (235 mg, 2.40 mmol) and a magnetic stir bar and was kept in vacuum for 10 min. After three nitrogen-vacuum cycles, a stock solution of Pd(dippf)male-imide (3.11 mg, 0.005 mmol) and dippf (2.13 mg, 0.005 mmol) in dry, distilled toluene (2 mL) was added *via*

Table 3. Highly selective synthesis of tertiary amines.^[a]



^[a] The residue originating from the aryl halide (Ar³-X) is placed on the right-hand side. *Conditions:* 1.00 mmol amine, 1.00 mmol Ar¹-Br, 2.40 mmol NaO-t-Bu, 0.5 mol% 6, 0.5 mol% dippf, 2 mL toluene, 80 °C, 20 h. Then 1.10 mmol Ar³-X in 0.5 mL toluene, 120 °C, 24 h, isolated yields.

syringe. The reaction mixture was stirred at 80 °C for 20 h, followed by addition of a solution of the second aryl halide (1.10 mmol) in toluene (0.5 mL) *via* syringe. The temperature was increased to 120 °C and stirring was continued for another 24 h. The mixture allowed to cool to room temperature and diluted with dichloromethane (30 mL) and water (30 mL). The aqueous layer was separated and extracted with dichloromethane (2×20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum (40 °C, 500 mbar). The crude product was further purified by flash chromatography (basic Al₂O₃, hexane/ethyl acetate), yielding the corresponding tertiary amine; yield: 75–96%.

Acknowledgements

We thank J. Tang for helpful discussion, the Chinese Scholarship Council (fellowship to F.J.), and A. Leidner for technical assistance.

References

- a) Y. Shirota, J. Mater. Chem. 2000, 10, 1–25; b) U. Mitschke, P. Bäuerle, J. Mater. Chem. 2000, 10, 1471– 1507; c) L. S. Hung, C. H. Chen, Mater. Sci. Eng. R Rep. 2002, 39, 143–222; d) P. Strohriegl, J. V. Grazulevicius, Adv. Mater. 2002, 14, 1439–1452.
- [2] C. W. Tang, S. A. VanSlyke, *Appl. Phys. Lett.* **1987**, *51*, 913–915.
- [3] a) B. W. D'Andrade, S. R. Forrest, *Adv. Mater.* 2004, *16*, 1585–1595; b) K. T. Kamtekar, A. P. Monkman, M. R.

Bryce, *Adv. Mater.* **2010**, *22*, 572–582; c) Y.-L. Chang, Z.-H. Lu, *J. Disp. Technol.* **2013**, *9*, 459–468; d) H. Sasabe, J. Kido, *J. Mater. Chem. C* **2013**, *1*, 1699–1707.

- [4] L. Akcelrud, Prog. Polym. Sci. 2003, 28, 875–962.
- [5] a) S. R. Forrest, *Chem. Rev.* 1997, 97, 1793–1896;
 b) S. R. Forrest, *Nature* 2004, 428, 911–918.
- [6] For selected examples see: a) K. R. Justin Thomas, J. T. Lin, Y.-T. Tao, C.-W. Ko, J. Am. Chem. Soc. 2001, 123, 9404–9411; b) J. Li, C. Ma, J. Tang, C.-S. Lee, S. Lee, Chem. Mater. 2005, 17, 615–619; c) V. Promarak, M. Ichikawa, T. Sudyoadsuk, S. Saengsuwan, S. Jungsuttiwong, T. Keawin, Synth. Met. 2007, 157, 17–22; d) M. Xu, C. Yi, C.-J. Yang, J.-H. Wang, Y.-Z. Liu, B. Xie, X.-C. Gao, P. Wang, D.-C. Zou, Thin Solid Films 2008, 516, 7720–7726; e) W. Gao, S. Wang, Y. Xiao, X. Li, Spectrochim. Acta A. Mol. Biomol. Spectrosc. 2012, 98, 215–221; f) S.-Y. Lee, Y.-H. Kwak, B.-W. Park, D.-Y. Shin, K.-H. Lee, H.-I. Jeong, S.-I. Kho, M.-H. Park, (Samsung Mobile Display Co., Ltd.), U.S. Patent 2013/0032788 A1, 2013.
- [7] For selected examples see: a) J. Salbeck, N. Yu, J. Bauer, F. Weissörtel, H. Bestgen, *Synth. Met.* 1997, 91, 209–215; b) U. Bach, K. De Cloedt, H. Spreitzer, M. Grätzel, *Adv. Mater.* 2000, 12, 1060–1063; c) K.-T. Wong, Z.-J. Wang, Y.-Y. Chien, C.-L. Wang, *Org. Lett.* 2001, 3, 2285–2288; d) R. D. Hreha, C. P. George, A. Haldi, B. Domercq, M. Malagoli, S. Barlow, J.-L. Brédas, B. Kippelen, S. R. Marder, *Adv. Funct. Mater.* 2003, 13, 967–973; e) M.-G. Shin, K. Thangaraju, S.-O. Kim, J.-W. Park, Y.-H. Kim, S.-K. Kwon, *Org. Electron.* 2011, 12, 785–793.
- [8] For reviews see: a) J. F. Hartwig, Acc. Chem. Res. 2008, 41, 1534–1544; b) J. F. Hartwig, Nature 2008, 455, 314– 322; c) D. S. Surry, S. L. Buchwald, Angew. Chem. 2008,

120, 6438–6461; *Angew. Chem. Int. Ed.* **2008**, *47*, 6338–6361; d) D. S. Surry, S. L. Buchwald, *Chem. Sci.* **2011**, *2*, 27–50.

[9] For selected examples see: a) F. Rataboul, A. Zapf, R. Jackstell, S. Harkal, T. Riermeier, A. Monsees, U. Dingerdissen, M. Beller, Chem. Eur. J. 2004, 10, 2983-2990; b) S. Urgaonkar, J. G. Verkade, J. Org. Chem. 2004, 69, 9135-9142; c) B. P. Fors, D. A. Watson, M. R. Biscoe, S. L. Buchwald, J. Am. Chem. Soc. 2008, 130, 13552-13554; d) B. P. Fors, P. Krattiger, E. Strieter, S. L. Buchwald, Org. Lett. 2008, 10, 3505-3508; e) Q. Shen, T. Ogata, J. F. Hartwig, J. Am. Chem. Soc. 2008, 130, 6586-6596; f) Q. Shen, J. F. Hartwig, Org. Lett. 2008, 10, 4109-4112; g) C. V. Reddy, J. V. Kingston, J. G. Verkade, J. Org. Chem. 2008, 73, 3047-3062; h) B. P. Fors, S. L. Buchwald, J. Am. Chem. Soc. 2010, 132, 15914-15917; i) B. J. Tardiff, R. McDonald, M. J. Ferguson, M. Stradiotto, J. Org. Chem. 2012, 77, 1056-1071; j) M. Pompeo, J. L. Farmer, R. D. J. Froese, M. G. Organ, Angew. Chem. 2014, 126, 3287–3290; Angew. Chem. Int. Ed. 2014, 53, 3223-3226; k) S. Sharif, R. P. Rucker, N. Chandrasoma, D. Mitchell, M. J. Rodriguez, R. D. J. Froese, M. G. Organ, *Angew. Chem.* 2015, *127*, 9643–9647; *Angew. Chem. Int. Ed.* 2015, *54*, 9507–9511.
[10] See the Supporting Information (Table S2) for details.

- [11] a) T. J. Colacot, H. A. Shea, Org. Lett. 2004, 6, 3731–3734; b) M. Murata, S. L. Buchwald, Tetrahedron 2004, 60, 7397–7403; c) A. Klapars, K. R. Campos, C.-Y. Chen, R. P. Volante, Org. Lett. 2005, 7, 1185–1188; d) E. Alvaro, J. F. Hartwig, J. Am. Chem. Soc. 2009, 131, 7858–7868; e) A. DeAngelis, T. J. Colacot, C. C. C. J. Seechurn, H. Li, T. J. Colacot in: New Trends in Cross-Coupling: Theory and Applications, (Ed.: T. J. Colacot), RSC Publishing, Cambridge, 2015, pp 20–138.
- [12] CCDC 1056399 contains 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.
- [13] See the Supporting Information for details.
- [14] a) H. Aziz, Z. D. Popovic, *Chem. Mater.* 2004, *16*, 4522–4532; b) F. So, D. Kondakov, *Adv. Mater.* 2010, *22*, 3762–3777; c) S. Schmidbauer, A. Hohenleutner, B. König, *Adv. Mater.* 2013, *25*, 2114–2129.
- [15] See the Supporting Information for details.