DOI: 10.1002/adsc.200800733

Increasing the Scope of Palladium-Catalyzed Cyanations of Aryl Chlorides

Thomas Schareina,[a] Ralf Jackstell,[a] Thomas Schulz,[a] Alexander Zapf,[a]
Alain Cotté,[b] Matthias Gotta,[b] and Matthias Beller[a,]*

[a] Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert-Einstein-Str. 29 A, 18059 Rostock, Germany
Fax: (+49)-381-1281-5000; e-mail: Matthias.Beller@catalysis.de
[b] Saltigo GmbH, Building H5 ZeTO 2, 51369 Leverkusen, Germany

Received: November 26, 2008; Published online: February 18, 2009

Abstract: An improved protocol for the palladium-catalyzed cyanation of electron-rich aryl chlorides with potassium ferrocyanide {$K_4[Fe(CN)_6]$} is presented. Compared to previous procedures the substrate scope is significantly broadened.

Keywords: aromatic substitution; aryl halides; C–C coupling; cyanides; palladium

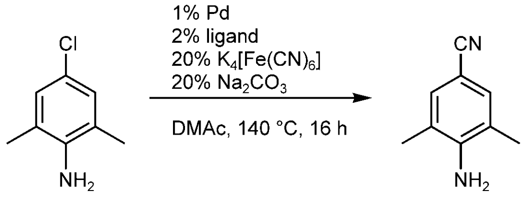
Introduction

In the last decade the use of palladium- and copper-catalyzed coupling reactions has proven to be a powerful tool for the functionalization of arenes and heteroarenes.[1] Obviously, the general applicability of a given coupling reaction both in academia and industry is based mainly on a broad substrate scope and the availability of starting materials, ligands, and catalysts. Due to efficient developments in the last decades most coupling reactions of undemanding bromo- and iodoarenes proceed smoothly and numerous catalysts based on palladium and in some cases on copper are known for these transformations. However, there exists still a number of interesting substrates for the pharmaceutical and agrochemical industry, which pose a significant challenge. For example, functionalized electron-rich aryl chlorides are desired substrates for various cross-coupling reactions. Unfortunately, at the same time, they constitute the most challenging substrates due to the high dissociation energy of the $C(sp^2)$–Cl bond,[2] and it is generally accepted that electron-rich derivatives react more slowly than electron-poor ones.[3]

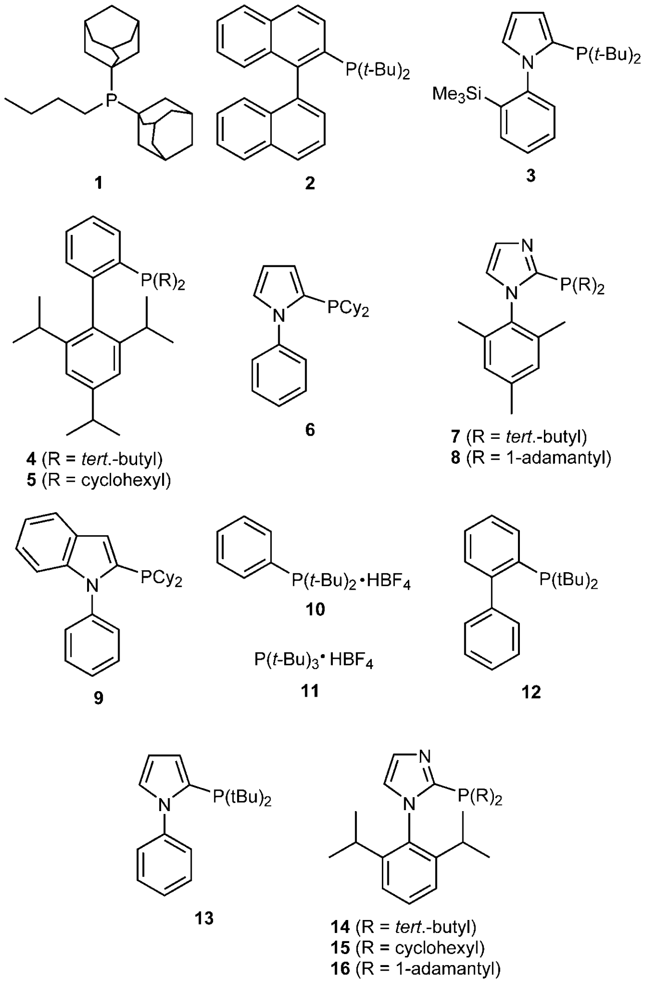
Here, we report improved palladium catalysts based on bulky heterocyclic phosphines, which allow for efficient cyanations of “difficult” aryl chlorides with potassium ferrocyanide. In recent years the synthesis of benzonitriles *via* palladium- and copper-catalyzed cyanations has gained considerable attention.[4,5] In 2004, we introduced potassium ferrocyanide $K_4[Fe(CN)_6]$ as a novel cyanation reagent, which is interesting both because of its price and low toxicity.[6,7] In fact, $K_4[Fe(CN)_6]$ is the most environmentally benign cyanation source known to date and quickly attracted substantial interest for various synthetic applications.[8] In addition to its environmental advantages, it allows for improved catalyst productivity and substrate scope. For example, catalyst turnover numbers of 18,000 are achieved without any ligand added in the palladium-catalyzed reaction of relatively simple aryl bromides.[6b] Using copper as catalyst metal in the presence of 1-alkylimidazoles as additives functionalized aryl and heteroaryl bromides were converted in high yields,[9] however aryl chlorides reacted only in rare cases. Nevertheless, initial success in the cyanation of aryl chlorides has been achieved. Sakakibara et al. have reported about nickel-based cyanation reactions, unfortunately HMPA was found as the best solvent.[10] More recently, we reported the use of $Pd(OAc)_2$/*n*-butyl-di(1-adamantyl)phosphine (Scheme 2, ligand **1**) for reactions of aryl chlorides with non-reactive substituents.[11] Most currently, Littke and coworkers described the use of 4 mol% Pd and 8 mol% of a special Buchwald-type ligand (Scheme 2, ligand **2**), Zn as additive, and $Zn(CN)_2$ as cyanide source.[12] So far, the use of palladium as catalyst metal seems indispensable for the conversion of aryl chlorides.

Results and Discussion

Primary anilines and phenols are demanding substrates for all kinds of C–C coupling reactions, since they may form C–N or C–O bonds. In addition, amino and hydroxy groups are known to act as ligands, blocking the reactive centre. In order to develop improved catalysts, 4-chloro-2,6-dimethylaniline was chosen as a substrate of medium difficulty. The respective cyanation served as a model reaction to



Scheme 1. Model reaction.



Scheme 2. Ligands tested.

study the influence of temperature, Pd content and different ligands (Scheme 1; Table 1). According to our previous work a high-boiling, polar solvent, temperatures of 140 °C and dried potassium hexacyanoferrate(II) were used in the presence of the sterically hindered heteroarylphosphine **3**.

Initial variations of the palladium source showed that $PdCl_2$, Na_2PdCl_4, and $Pd(TFA)_2$ gave better results than $Pd_2(dba)_3$ and Pd(allyl)Cl. The low performance of $Pd(OAc)_2$ corresponds with the findings of Littke et al.[12] For reasons of practicability $Pd(TFA)_2$ was used further on, since stock solutions are easily prepared.

It should be noted that the reaction is highly sensitive with respect to the amount and type of base. Hence, changing from sodium carbonate to standard inorganic bases commonly used in coupling reactions led to significantly lower yields (Table 1, entries 7–10). Even the concentration of base is important (Table 1, entry 11), despite the fact that, for purely stoichiometric reasons, no base is needed. However, in the absence of sodium carbonate no conversion is observed (Table 1, entry 12). This suggests that the base is involved in the formation of the reactive intermediate.

Among the tested solvents NMP gave comparable results to the standard solvent DMAc (Table 1, entries 13–16). Although the use of potassium hexacyanoferrate(II) hydrate was found to be advantageous in some cases,[11,13] in this model reaction a major decrease of the yield occurred (Table 1, entry 19). Moreover, potassium hexacyanoferrate(III) was tested, but also with low success (Table 1, entry 20).

Next, the influence of different electron-rich ligands was investigated. Selected results are shown in Table 2. A special focus has been given on biaryl-substituted ligands.[14,15] As a general trend, dicyclohexyl-substituted phosphines were not suitable, while di-*tert.*-butyl-substituted and di-1-adamantyl-substituted biarylphosphines led to higher yields. However, this is difficult to understand and we have no conclusive explanation why, e. g., *t*-Bu-XPhos (Scheme 2, ligand **4**) performed poorly, while the nominally less bulky *tert.*-butyl-JohnPhos (Scheme 2, ligand **12**) gave a yield of 59%.

Finally, the novel protocol has been proven successful for the cyanation of diverse electron-rich and challenging aryl chlorides. Selected results of the scope and limitations are shown in Table 3. In general, only the two best results were included. It should be noted that for certain substrates a proper adaption of the reaction conditions might further improve the yield. For 2-, 3-, and 4-chloroanisole (Table 3, entries 1–6) and 5-chloro-1,3-benzodioxole (Table 3, entries 7 and 8), ligand **11** (tri-*tert.*-butylphosphine) gave the best results (48–83% yield), while imidazole-substituted ligands **14** and **15** led to 18–85% yield. With the differently substituted chloroanilines the new bulky phosphine ligands **14–16** based on a heterocyclic framework dominate leading to yields of 40–75% of the corresponding benzonitrile. Notably, also free phenols can be cyanated in significant to good yield in the presence of the “right” ligand (Table 3, entries 19–21). And last but not least, with the sterically most hindered 2,6-dimethylchlorobenzene the best result is obtained in the presence of **1** (Table 3, entries 22 and 23).[11]

Table 1. Cyanation of 4-chloro-2,6-dimethylaniline.[a]

Entry	Solvent	*T* [°C]	Metal Precursor (mol% Pd)	Base (mol)	Conversion[b] [%]	Yield[b] [%]
1	**DMAc[c]**	**140**	**Pd(TFA)$_2$ (1)**	**Na_2CO_3 (20)**	**82**	**61**
2	DMAc	140	$Pd_2(dba)_3$ (1)	Na_2CO_3 (20)	65	50
3	**DMAc**	**140**	**$PdCl_2$ (1)**	**Na_2CO_3 (20)**	**78**	**66**
4	**DMAc**	**140**	**Na_2PdCl_4 (1)**	**Na_2CO_3 (20)**	**75**	**65**
5	DMAc	140	$Pd(OAc)_2$ (1)	Na_2CO_3 (20)	72	28
6	DMAc	140	Pd(allyl)Cl (1)	Na_2CO_3 (20)	33	26
7	DMAc	140	Pd(TFA)$_2$ (1)	K_2CO_3 (20)	61	13
8	DMAc	140	Pd(TFA)$_2$ (1)	Cs_2CO_3[d] (20)	52	6
9	DMAc	140	Pd(TFA)$_2$ (1)	K_3PO_4[d] (20)	38	15
10	DMAc	140	Pd(TFA)$_2$ (1)	KF[d] (20)	33	21
11	DMAc	140	Pd(TFA)$_2$ (1)	Na_2CO_3 (50)	39	30
12	DMAc	140	Pd(TFA)$_2$ (1)	–	2	0
13	DMSO[c]	140	Pd(TFA)$_2$ (1)	Na_2CO_3 (20)	30	20
14	**NMP[c]**	**140**	**Pd(TFA)$_2$ (1)**	**Na_2CO_3 (20)**	**59**	**59**
15	DMF[c]	140	Pd(TFA)$_2$ (1)	Na_2CO_3 (20)	30	20
16	dioxane[c]	140	Pd(TFA)$_2$ (1)	Na_2CO_3 (20)	28	11
17	DMAc	120	Pd(TFA)$_2$ (1)	Na_2CO_3 (20)	71	54
18	DMAc	160	Pd(TFA)$_2$ (1)	Na_2CO_3 (20)	44	37
19[e]	DMAc	140	Pd(TFA)$_2$ (1)	Na_2CO_3 (20)	12	6
20[f]	DMAc	140	Pd(TFA)$_2$ (1)	Na_2CO_3 (20)	29	22

[a] *General reaction conditions:* 2 mmol 4-chloro-2,6-dimethylaniline, 2 mol% ligand **3**, 20 mol% $K_4[Fe(CN)_6]$, 2 mL solvent, 100 μL tetradecane (internal standard for GC), other compounds and temperature as given in the table, heated for 16 h.

[b] Conversion and yield determined by GC as the average of two experiments.

[c] All solvents were dried by standard procedures. DMAc = *N*,*N*-dimethylacetamide, DMSO = dimethyl sulfoxide, NMP = *N*-methylpyrrolidone, dioxane = 1,4-dioxane.

[d] Stored and weighed in a glove box under argon.

[e] $K_3[Fe(CN)_6]$ (20) instead of $K_4[Fe(CN)_6]$.

[f] $K_4[Fe(CN)_6]\cdot 3H_2O$ (20) instead of $K_4[Fe(CN)_6]$.

Table 2. Influence of ligands on the cyanation of 4-chloro-2,6-dimethylaniline (table is ordered by ascending yield).[a]

	Ligand[b] (mol%)	Conversion[c] [%]	Yield[c] [%]
1	**4** (2)	10	7
2	**5** (2)	17	10
3	**1** (2)	24	16
4	**2** (2)	30	18
5	**6** (2)	25	20
6	**7** (2)	30	22
7	**9** (2)	30	25
8	**10** (2)	35	26
9	**11** (2)	77	59
10	**12** (2)	79	59
11	**13** (2)	76	63
12	**8** (2)	95	73
13	**14** (2)	91	75

[a] *General conditions:* 2 mmol 4-chloro-2,6-dimethylaniline, 2 mol% ligand, 20 mol% $K_4[Fe(CN)_6]$, 2 mL DMAc, 100 μL tetradecane (internal standard for gc), 20 mol% Na_2CO_3, 140 °C, 16 h.

[b] Conversion and yield determined by GC as the average of two experiments.

Conclusions

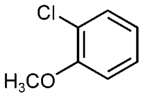
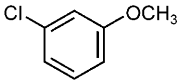
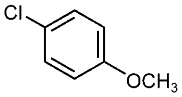
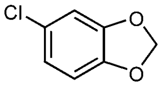
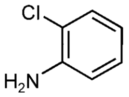
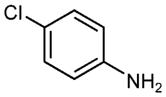
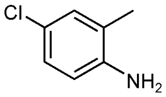
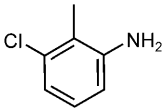
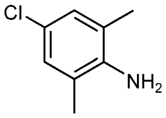
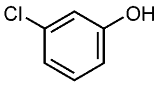
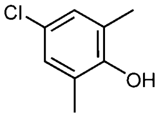
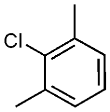
In summary, we have shown that electron-rich aryl chlorides can be successfully converted to benzonitriles in the presence of palladium/phosphine catalysts applying the environmentally benign cyanide source $K_4[Fe(CN)_6]$. Of special importance is the cyanation of difficult substrates such as chlorophenols and chloroanilines. Nevertheless, so far one universally applicable catalyst system for the cyanation of aryl chlorides is not yet available. In this respect the novel bulky heterocyclic phosphine ligands represent a variable class of phosphine ligands, which are easily tunable and show good prospects not only for cyanation reactions, but also for other cross-coupling reactions of aryl chlorides.[16]

Experimental Section

General Procedures

$K_4[Fe(CN)_6]\cdot 3H_2O$ was ground to a fine powder and dried under vacuum (*ca.* 2 mbar) at 80 °C overnight. This material was stored in a stoppered bulb and could be used for

Table 3. Cyanation of various electron-rich aryl chlorides.[a]

Entry	Substrate	Solvent	Metal Precursor (mol% Pd)	Ligand (mol%)	Conversion [%]	Yield [%]
1		DMAc	Pd(TFA)$_2$ (1)	**11** (2)	48	48
2		DMAc	Pd(TFA)$_2$ (1)	**14** (2)	20	18
3		DMAc	Pd(TFA)$_2$ (1)	**11** (2)	90	83
4		DMAc	Pd(TFA)$_2$ (1)	**15** (2)	76	68
5		DMAc	Pd(TFA)$_2$ (1)	**3** (2)	90	85
6		DMAc	Pd(TFA)$_2$ (1)	**11** (2)	83	83
7		DMAc	Pd(TFA)$_2$ (1)	**14** (2)	60	58
8		DMAc	Pd(TFA)$_2$ (1)	**11** (2)	52	52
9		DMAc	PdCl$_2$ (1)	**15** (2)	75	55
10		DMAc	Pd(TFA)$_2$ (1)	**14** (2)	78	40
11		DMAc	Pd(TFA)$_2$ (1)	**11** (2)	73	54
12		DMAc	Pd(TFA)$_2$ (1)	**16** (2)	84	45
13		NMP	Pd(TFA)$_2$ (1)	**3** (2)	73	67
14		DMAc	Pd(TFA)$_2$ (1)	**16** (2)	69	59
15		DMAc	Pd(TFA)$_2$ (1)	**16** (2)	84	65
16		DMAc	Pd(TFA)$_2$ (1)	**14** (2)	75	49
17		DMAc	Pd(TFA)$_2$ (1)	**14** (2)	91	75
18		DMAc	Pd(TFA)$_2$ (1)	**8** (2)	95	73
19		DMAc	Pd(TFA)$_2$ (1)	**11** (2)	63	44
20		DMAc	Pd(TFA)$_2$ (1)	**3** (2)	78	61
21		DMAc	Pd(TFA)$_2$ (1)	**14** (2)	77	60
22		DMAc	Pd(TFA)$_2$ (1)	**1** (2)	87	76
23		DMAc	Pd(TFA)$_2$ (1)	**16** (2)	43	37

[a] *General reaction conditions:* 2 mmol aryl chloride, 2 mol% ligand, 20 mol% $K_4[Fe(CN)_6]$, 2 mL DMAc, 100 μL tetradecane (internal standard for GC), 20 mol% Na_2CO_3, 140 °C, 16 h.

months without noticeable decreases in activity. NMP and DMAc were distilled from CaH_2 under reduced pressure and stored under argon. DMSO was fractionally distilled under reduced pressure. Dioxane was dried over sodium benzophenone ketyl, distilled and stored under argon. Ligands **1**, **2**, **4**–**6** and **9**–**13** are commercially available. Ligands **3** (see below), **7**,[15a] **8**,[16] **14**–**16**[16] were available as test samples in our group. All other materials were purchased from different chemicals providers (Aldrich, Fluka, Alfa-Aesar etc.) and used as received.

Data of ligand 3 {2-(di-*tert.*-butylphosphino)-1-[2-(trimethylsilyl)phenyl]-1*H*-pyrrole}: ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 0.00 [s, 9 H, Si(CH$_3$)$_3$], 1.80 {d, 18 H, P[C(CH$_3$)$_3$]$_2$}, 6.6 (d, 1 H), 6.8 (d, 1 H), 7.2 (m, 2 H), 7.40–7.50 (m, 3 H); ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 0.0, 30.6, 33.1, 117.4, 118.8, 128.3, 130.5, 134.9, 138.3, 142.7; HR-MS: *m/z* = 359.21875, calcd. for $C_{21}H_{34}NPSi$: 359.21982.

Typical Catalytic Procedure

148 mg (0.4 mmol) dry $K_4[Fe(CN)_6]$, base, palladium source, ligand, and 2 mmol aryl chloride were placed in an Ace pressure tube under argon. Thereafter, 100 μL tetradecane (internal standard for GC) and 2 mL solvent were added and the mixture was stirred for 1 min. The pressure tube was sealed and heated for 16 h at the temperature specified in the tables. After cooling to room temperature 3 mL ethyl acetate were added and the mixture was analyzed by GC. Conversion and yield were calculated as average of 2 parallel runs. For isolation of the products the reaction mixture was transferred to a separation funnel with the help of an appropriate non-water miscible solvent and washed with water. In experiments with >10 mmol of substance often a dark bluish precipitate and emulsions were formed, which conceal the interface and lengthen the work-up. In these cases, a filtration over a sintered glass frit removes both. The organic phase was dried over Na_2SO_4. After evaporation of the solvents the residue was subjected to column chromatography (silica, hexane/ethyl acetate). All known benzonitriles were identified by comparison with commercially available materials and literature data.

References

[1] Selected recent reviews of Pd-catalyzed coupling reactions see: a) A. Frisch, M. Beller, *Angew. Chem.* **2005**, *117*, 680–695; *Angew. Chem. Int. Ed.* **2005**, *44*, 674–688; b) A. Zapf, M. Beller, *Chem. Commun.* **2005**, 431–440; c) C. Barnard, *Platinum Met. Rev. Platinum Metals Rev.* **2008**, *52*, 38–45; d) A. Fihri, P. Meunier, J.-C. Hierso, *Coord. Chem. Rev.* **2007**, *251*, 2017–2055; e) N. T. S. Phan, M. V. D. Sluys, C. W. Jones, *Adv. Synth. Catal.* **2006**, *348*, 609–679; f) O. Reiser, *Angew. Chem.* **2006**, *118*, 2904–2906; *Angew. Chem. Int. Ed.* **2006**, *45*, 2838–2840; g) K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem.* **2005**, *117*, 4516–4563; *Angew. Chem. Int. Ed.* **2005**, *44*, 4442–4489.

[2] The dissociation energy of the $C(sp^2)$–Cl bond is considerably higher compared to the corresponding Br- or I-aromatic compounds (C–Cl 402, C–Br 339, C–I 272 $kJ\,mol^{-1}$); see: V. V. Grushin, H. Alper, *Chem. Rev.* **1994**, *94*, 1047–1062.

[3] T. H. Riermeier, A. Zapf, M. Beller, *Top. Catal.* **1997**, *4*, 301–309.

[4] For reviews see: a) M. Sundermeier, A. Zapf, M. Beller, *Eur. J. Inorg. Chem.* **2003**, 3513–3526; b) T. Schareina, A. Zapf, A. Cotté, N. Müller, M. Beller, *Synthesis* **2008**, 3351–3355.

[5] a) D. M. Tschaen, R. Desmond, A. O. King, M. C. Fortin, B. Pipik, S. King, T. R. Verhoeven, *Synth. Commun.* **1994**, *24*, 887–890; b) M. Sundermeier, A. Zapf, M. Beller, J. Sans, *Tetrahedron Lett.* **2001**, *42*, 6707–6710; c) J. Ramnauth, N. Bhardwaj, P. Renton, S. Rakhit, S. P. Maddaford, *Synlett* **2003**, 2237–2239; d) M. Sundermeier, A. Zapf, M. Beller, *Angew. Chem.* **2003**, *115*, 1700–1703; *Angew. Chem. Int. Ed.* **2003**, *42*, 1661–1664; e) M. Sundermeier, S. Mutyala, A. Zapf, A. Spannenberg, M. Beller, *J. Organomet. Chem.* **2003**, *684*, 50–55; f) M. Sundermeier, A. Zapf, M. Sateesh, M. Beller, *Chem. Eur. J.* **2003**, *9*, 1828–1836; g) H. R. Chobanian, B. P. Fors, L. S. Lin, *Tetrahedron Lett.* **2006**, *47*, 3303–3306; h) R. S. Jensen, A. S. Gajare, K. Toyota, M. Yoshifuji, F. Ozawa, *Tetrahedron Lett.* **2005**, *46*, 8645–8648; i) J. M. Veauthier, C. N. Carlson, G. E. Collis, J. L. Kiplinger, K. D. John, *Synthesis* **2005**, 2683–2686; j) R. Chidambaram, *Tetrahedron Lett.* **2004**, *45*, 1441–1444; k) H. J. Cristau, A. Ouali, J. F. Spindler, M. Taillefer, *Chem. Eur. J.* **2005**, *11*, 2483–2492; l) B. Tylleman, R. Gomez-Aspe, G. Gbabode, Y. H. Geerts, S. Sergeyev, *Tetrahedron* **2008**, *64*, 4155–4161; m) P. Ryberg, *Org. Process Res. Dev.* **2008**, *12*, 540–543; n) Z. Iqbal, A. Lyubimtsev, M. Hanack, *Synlett* **2008**, 2287–2290; o) S. Challenger, Y. Dessi, D. E. Fox, L. C. Hesmondhalgh, P. Pascal, A. J. Pettman, J. D. Smith, *Org. Process Res. Dev.* **2008**, *12*, 575–583; p) R. R. Srivastava, A. J. Zych, D. M. Jenkins, H. J. Wang, Z. J. Chen, D. J. Fairfax, *Synth. Commun.* **2007**, *37*, 431–438; q) P. Dolakova, M. Masojidkova, A. Holy, *Heterocycles* **2007**, *71*, 1107–1115; r) X. Wang, B. Zhi, J. Baum, Y. Chen, R. Crockett, L. Huang, S. Eisenberg, J. Ng, R. Larsen, M. Martinelli, P. Reider, *J. Org. Chem.* **2006**, *71*, 4021–4023; s) M. T. Martin, B. Liu, B. E. Cooley, J. F. Eaddy, *Tetrahedron Lett.* **2007**, *48*, 2555–2557; *cf.* also ref.[8]

[6] a) T. Schareina, A. Zapf, M. Beller, *Chem. Commun.* **2004**, 1388–1389; b) T. Schareina, A. Zapf, M. Beller, *J. Organomet. Chem.* **2004**, *689*, 4576–4583.

[7] Other cyanation sources, for example, KCN [LD_{Lo} (oral, human) = 2.86 $mg\,kg^{-1}$], are highly poisonous, $K_4[Fe(CN)_6]$ is essentially non-toxic {the LD_{50} of $K_4[Fe(CN)_6]$ is lower than that for NaCl}. $K_4[Fe(CN)_6]\cdot 3\,H_2O$ is used as an anti-agglutinating agent in table salt, as an agent for the removal of metal traces from wine, and it is used in chemistry experimental kits for adolescents (at least in Germany and the EU). Toxicity data taken from safety data sheets of the corresponding compounds available from Merck KGaA, http://www.merck-chemicals.de.

[8] a) B. Mariampillai, J. Alliot, M. Li, M. Lautens, *J. Am. Chem. Soc.* **2007**, *129*, 15372–15379; b) B. Mariampillai, D. Alberico, V. Bidau, M. Lautens, *J. Am. Chem. Soc.* **2006**, *128*, 14436–14437; c) A. Pinto, Y. X. Jia, L. Neuville, J. P. Zhu, *Chem. Eur. J.* **2007**, *13*, 961–967; d) Y. Z. Zhu, C. Cai, *Eur. J. Org. Chem.* **2007**, 2401–2404; e) Y. Z. Zhu, C. Cai, *J. Chem. Res. S.* **2007**, 484–485; f) Y. N. Cheng, Z. Duan, T. Li, Y. J. Wu, *Synlett* **2007**, 543–546; g) G. Chen, J. Weng, Z. C. Zheng, X. H. Zhu, Y. Y. Cai, J. W. Cai, Y. Q. Wan, *Eur. J. Org. Chem.* **2008**, 3524–3528; h) Y. Z. Zhu, C. Cai, *Synth. Commun.* **2008**, *38*, 2753–2760; i) N. S. Nandurkar, B. M. Bhanage, *Tetrahedron* **2008**, *64*, 3655–3660; j) V. Polshettiwar, P. Hesemann, J. J. E. Moreau, *Tetrahedron* **2007**, *63*, 6784–6790; k) Z. Li, S. Y. Shi, J. Y. Yang, *Synlett* **2006**, 2495–2497.

[9] a) T. Schareina, A. Zapf, W. Mägerlein, N. Müller, M. Beller, *Chem. Eur. J.* **2007**, *13*, 6249–6254; b) T. Schareina, A. Zapf, W. Mägerlein, N. Müller, M. Beller, *Synlett* **2007**, 555–558; c) T. Schareina, A. Zapf, M. Beller, *Tetrahedron Lett.* **2005**, *46*, 2585–2588.

[10] a) Y. Sakakibara, F. Okuda, A. Shimoyabashi, K. Kirino, M. Sakai, N. Uchino, K. Takagi, *Bull. Chem.

Soc. Jpn. **1988**, *61*, 1985–1990; b) Y. Sakakibara, Y. Ido, K. Sasaki, M. Sakai, N. Uchino, *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2776–2778.

[11] T. Schareina, A. Zapf, W. Mägerlein, N. Müller, M. Beller, *Tetrahedron Lett.* **2007**, *48*, 1087–1090.

[12] A. Littke, M. Soumeillant, R. F. Kaltenbach, R. J. Cherney, C. M. Tarby, S. Kiau, *Org. Lett.* **2007**, *9*, 1711–1714.

[13] S. A. Weissman, D. Zewge, C. Chen, *J. Org. Chem.* **2005**, *70*, 1508–1510.

[14] For recent applications of Buchwald-type ligands see: a) J. Lemo, K. Heuze, D. Astruc, *Chem. Commun.* **2007**, 4351–4353; b) S. E. Denmark, C. R. Butler, *J. Am. Chem. Soc.* **2008**, *130*, 3690–3704; c) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.* **2008**, *108*, 3351–3378; d) U. Scholz, B. Schlummer, *Tetrahedron* **2005**, *61*, 6379–6385; e) B. Schlummer, U. Scholz, *Adv. Synth. Catal.* **2004**, *346*, 1599–1626; f) U. Schön, J. Messinger, M. Buckendahl, M. S. Prabhub, A. Konda, *Tetrahedron Lett.* **2007**, *48*, 2519–2525; g) B. P. Fors, D. A. Watson, M. R. Biscoe, S. L. Buchwald, *J. Am. Chem. Soc.* **2008**, *130*, 13552–13554; h) M. C. Willis, *Angew. Chem.* **2007**, *119*, 3470–3472; *Angew. Chem. Int. Ed.* **2007**, *46*, 3402–3404; i) T. E. Barder, M. R. Biscoe, S. L. Buchwald, *Organometallics* **2007**, *26*, 2183–2192; j) R. A. Altman, B. P. Fors, S. L. Buchwald, *Nat. Protoc.* **2007**, *2*, 2881–2887.

[15] For selected applications of aryl-heteroaryl phosphine ligands see: a) S. Harkal, F. Rataboul, A. Zapf, C. Fuhrmann, T. H. Riermeier, A. Monsees, M. Beller, *Adv. Synth. Catal.* **2004**, *346*, 1742–1748; b) F. Rataboul, A. Zapf, R. Jackstell, T. Riermeier, A. Monsees, U. Dingerdissen, M. Beller, *Chem. Eur. J.* **2004**, *10*, 2983–2990; c) N. Schwarz, A. Tillack, K. Alex, I. A. Sayyed, R. Jackstell, M. Beller, *Tetrahedron Lett.* **2007**, *48*, 2897–2900; d) N. Schwarz, A. Pews-Davtyan, K. Alex, A. Tillack, M. Beller, *Synthesis* **2007**, 3722–3730.

[16] a) T. Schulz, C. Torborg, B. Schäffner, J. Huang, A. Zapf, R. Kadyrov, A. Börner, M. Beller, *Angew. Chem.* **2009**, *121*, 936–939; *Angew. Chem. Int. Ed.* **2009**, *48*, 918–921; b) C. Torborg, J. Huang, T. Schulz, B. Schäffner, A. Zapf, A. Spannenberg, A. Börner, M. Beller, *Chem. Eur. J.* **2009**, *15*, 1329–1336.