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Small Substituents Make Large Differences: Aminopyrimidinyl Phosphanes Undergoing C–H Activation

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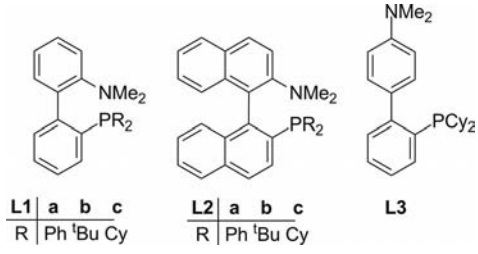
Palladium complexes synthesised from $(C_6H_5CN)_2PdCl_2$ and (2-aminopyrimidinyl)phosphanes show different coordination modes depending on the nature of the amino substituent attached to the pyrimidine ring. Whereas *P,N*-coordination is observed for primary and secondary amino groups, tertiary amino groups lead to C–H activation at the pyrimidine ring. These differences result in strongly different catalytic activities in the Suzuki–Miyaura coupling reaction. The palladium complexes were characterised spectroscopically and by means of X-ray structural analysis. DFT calculations were carried out to differ between the electronic and steric effects that are responsible for their behaviour in catalysis.

Introduction

The discovery of palladium complexes as catalysts for C–C bond formation turned out to be one of the fundamental advances in organic synthesis during the last years.[1] In 2010, it was highlighted by awarding the Nobel Prize to Heck,[2] Negishi[3] and Suzuki.[4] The Suzuki–Miyaura coupling is the key reaction for the formation of biaryls, a class of compounds that have found application in pharmaceuticals, optoelectronic devices and liquid crystal chemistry, to name just a few. Due to the broad availability of its substrates (arylbronic acids or borates and aryl halides or triflates) and its tolerance towards solvents and functional groups, the Suzuki–Miyaura coupling reaction has found widespread applications in synthetic organic chemistry.

Challenges associated with Suzuki reactions have focused on the use of unreactive arylchlorides as coupling partners[5] and in developing catalysts that efficiently perform under mild reaction conditions in combination with low catalyst loadings.[6] A remaining task is to achieve cross couplings under these mild conditions for highly hindered biaryl junctions.[7]

Generally, palladium phosphane complexes have been employed as catalysts for this reaction.[8] Some *P,N*-ligands have also been reported, but they often require longer reaction times, harsher reaction conditions, higher palladium loadings or a larger excess of ligand compared to pure phosphane donors. An outstanding example has been reported by Buchwald et al.; the dimethylamino-functionalised ligand **L1c** (Scheme 1) allows the palladium-catalysed Suzuki couplings of aryl chlorides at room temperature and the amination of unactivated aryl chlorides.[9] Kocovsky et al. reported a substantial acceleration of Suzuki couplings in the presence of ligand **L2a** (MAP).[10] They were also able to prove by X-ray crystal structural analysis that the MAP ligand coordinates to Pd through an unusual P,C_σ-chelation rather than by a *P,N*-binding mode.[11] Buchwald et al. reported that the palladium complexes of ligands **L2b**,**c** show excellent reactivities in asymmetric Suzuki couplings.[12] Faller et al. prepared and characterised two allyl palladium complexes of **L1** type ligands. They demonstrated that the preference for *P,N*- versus *P,C*-binding is controlled by subtle electronic and steric effects; *P,N*-binding is preferred in the Ph_2P case, whereas P,η^2(C1′–C6′)-binding is preferred for the Cy_2P analogue.[13] Vilar et al. reported that in the palladium complex of **L1b**[14] the ligand undergoes P,C_σ-chelation as **L2a**. Lakshman et al. reported a study on ligands **L3** and **L1a** for C–N and C–C bond formation.[15] **L3** bearing two vacant *ortho* positions turned out to be superior to **L1a**. They also obtained single crystals of a 1:1 complex of **L3** and $Pd(OAc)_2$ and found that C–H activation of the arene ring in the *ortho* position gives a cyclometallated product.



Scheme 1. Aminofunctionalised phosphanes for coupling reactions.

In this paper, we will show that slight changes in the substitution pattern of phosphane ligands bearing aminopyr-

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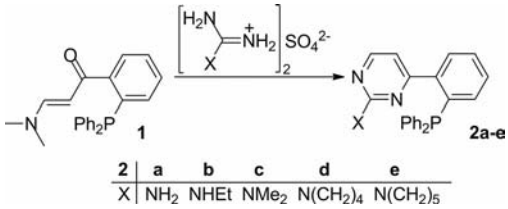
imidine units allows control over the coordination mode (*P*,*N* vs. *P*,*C*) of the corresponding palladium(II) complexes and furthermore leads to a pronounced difference in the catalytic activity (Suzuki–Miyaura coupling) of these palladium complexes.

Results and Discussion

Synthesis and Characterisation of Ligands and Complexes

Recently, we have been investigating the role of pyrazole derived ligands in homogeneous catalysis[16] and have developed a rapid access method to pyrazolylaryl-functionalised phosphanes through a fluoride-catalysed P–C coupling reaction.[17] Since precursor **1** (Scheme 2) also allows access of [(2-aminopyrimidin-4-yl)aryl]phosphanes on large scales with excellent yields, we were particularly interested in using this type of ligands for palladium-catalysed coupling reactions.



Scheme 2. Synthesis of 2-aminopyrimidin-4-yl-functionalised triphenylphosphanes.

Treatment of aminopropenone **1** with an excess of the appropriate guanidinium salt in ethanol under basic conditions gives the 2-aminopyrimidinyl-functionalised phosphanes **2a**–**e** in yields of ≥90%.

Recrystallisation of **2a** and **2e** from ethanol resulted in the formation of single crystals suitable for X-ray structural analysis. The results are presented in Figure 1. Whereas ligand **2e** shows the typical behaviour of organic compounds with weak intermolecular interactions, compound **2a** exhibits strong intermolecular hydrogen bonds between the amino group and the nitrogen atoms of the pyrimidine ring leading to a 1D "zig-zag" arrangement.

Reacting ligands **2a**–**b** – both bearing at least one proton at the amino nitrogen atom – with $(C_6H_5CN)_2PdCl_2$ in CH_2Cl_2 gave the expected the *P*,*N*-coordinated dichloropalladium(II) complexes **3a**,**b** (Scheme 3). In contrast, ligands **2c**–**e** – all bearing a tertiary amino group – led to C–H activation and thus to the cyclometallated products **4c**–**e**, which exist as zwitterions in the solid state. To best of our knowledge, this is a unique example of alternative *P*,*N*- and *P*,*C*-coordination modes in closely related palladium complexes.

For the ligands **2a**–**e**, the ^{1}H NMR spectroscopic resonances of the protons in the 5- (δ = 6.67–6.75 ppm) and 6-positions (δ = 8.16–8.33 ppm) of the pyrimidine ring are relatively independent from the nature of the amino substituent in the 2-position of the heterocycle. The ^{31}P NMR spectroscopic resonances of **2a**–**e** are observed between δ = –12.04 and –12.22 ppm, which is a slight shift to higher field compared with PPh_3. In contrast, the ^{1}H and ^{31}P NMR spectra of the palladium complexes **3a**,**b** and **4c**–**e** differ depending on the coordination mode; whereas for compounds **3a**,**b** there are typical doublets for the protons in the 5- and 6-positions at about δ = 6.88 and 8.26 ppm, respectively, a singlet at about δ = 8.52 ppm is observed for the C–H-activated complexes **4c**–**e** (see the Supporting Information).

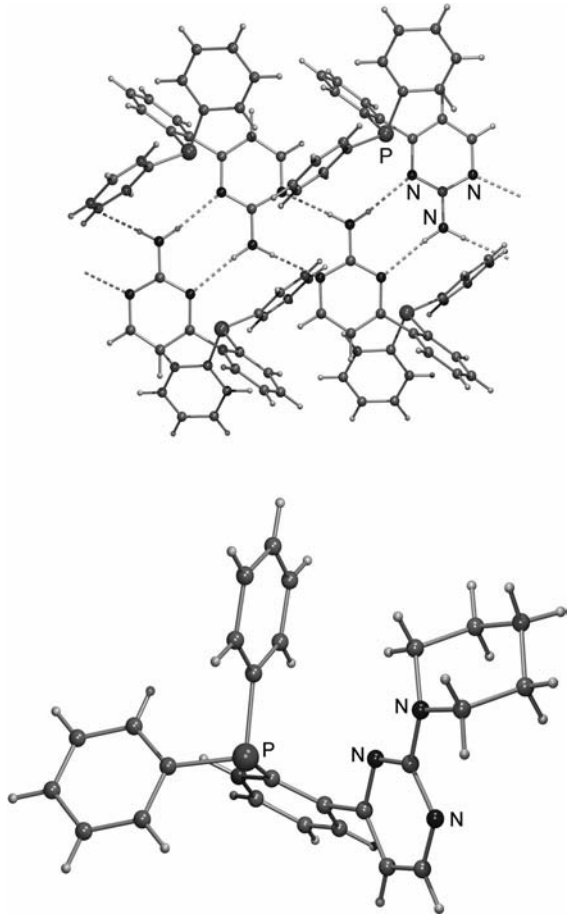
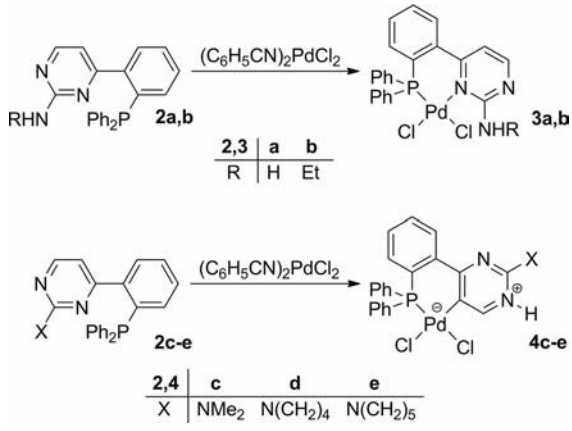


Figure 1. Molecular structures of ligands **2a** (top) and **2e** (bottom) in the solid state.



Scheme 3. Synthesis of palladium(II) complexes derived from 2-aminopyrimidin-4-yl-substituted triphenylphosphane ligands.

The ^{31}P NMR spectroscopic resonances of **4c**–**e** are shifted by about 1.0–1.5 ppm towards higher field with respect to **3a**,**b** indicating an increase of electron density at the palladium(II) centres due to the coordination of a carbanion in the *cis*-position to the phosphane donor.

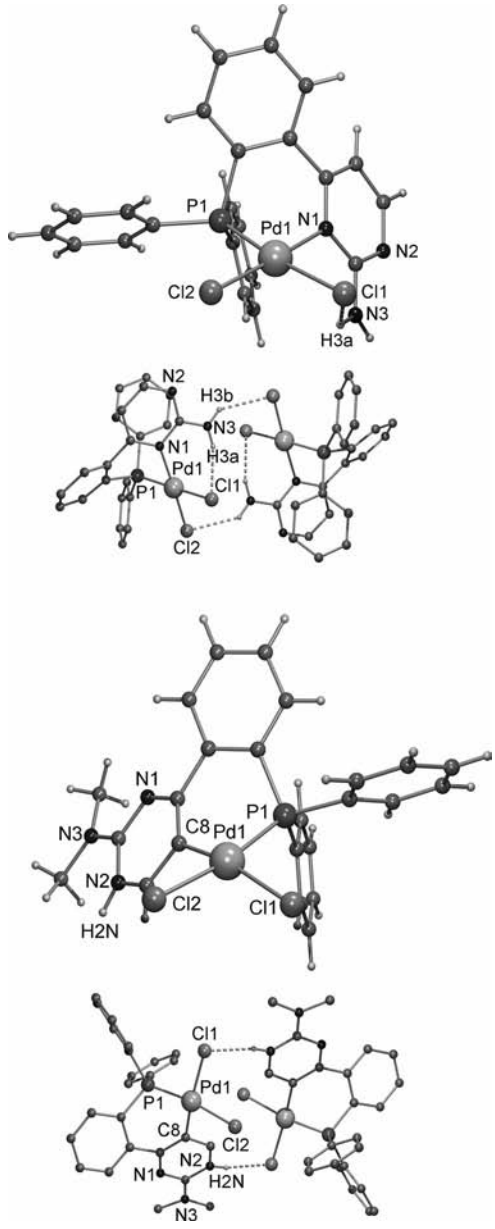


Figure 2. Molecular structures of the palladium complexes **3a** (top) and **4c** (bottom) in the solid state; dimers resulting due to the formation of intermolecular hydrogen bonds are also shown. Characteristic bond lengths [Å] and angles [°] for **3a**: Pd1–Cl1 2.3913(7), Pd1–Cl2 2.2915(7), Pd1–P1 2.2184(6), Pd1–N1 2.083(2), N3–H3A 0.90(2), H3A···Cl1 2.48(3), N3···Cl1 3.201(4), Cl1–Pd1–Cl2 90.98(3), Cl1–Pd1–P1 174.29(3), Cl1–Pd1–N1 93.35(6), Cl2–Pd1–P1 93.63(2), Cl2–Pd1–N1 175.52(6), P1–Pd1–N1 82.11(6), N3–H3A···Cl1 137(3). Characteristic bond lengths (Å) and angles [°] for **4c**: Pd1–Cl1 2.3885(9), Pd1–Cl2 2.3696(10), Pd1–P1 2.2118(9), Pd1–C8 2.016(4), N2–H2N 0.87(3), Cl1–Pd1–Cl2 90.14(3), Cl1–Pd1–P1 95.93(3), Cl1–Pd1–C8 165.91(10), Cl2–Pd1–P1 171.34(3), Cl2–Pd1–C8 91.56(10), P1–Pd1–C8 84.06(10).

Often C–H activation in the *ortho*-position of aromatic ligands requires basic reaction conditions [e.g., $Pd(OAc)_2$ as the Pd source]. Here, the much less reactive $PdCl_2$ fragment alone is capable of performing this reaction since the pyrimidine moiety acts like an internal base. Recrystallisation of compounds **3a** and **4c** by vapour diffusion from $CHCl_3$/*n*-hexane and DMSO/$CHCl_3$/diethyl ether, respectively, gave crystals suitable for single-crystal X-ray diffraction analysis (Figure 2).

In both complexes, the palladium centres are coordinated in a distorted square-planar geometry. They undergo intra- (**3a**: N3–H3A···Cl1) and intermolecular hydrogen bonding (**3a**: N3–H3B···Cl2a; **4c**: N2–HN2···Cl1a) leading to dimers in the solid state. The formation of dimers is probably the reason for the pronounced bending of the Cl1–Pd1–C8 axis (165.91°) in compound **4c**. Although there is only a slight difference in the Pd–P distances between the complexes, the Pd–C distance in **4c** (2.016 Å) is significantly shorter than the Pd–N distance in **3a** (2.083 Å), expressing increased covalency.

DFT calculations (B3LYP//6-31G*/LANL2DZ*) on compounds **3a** (APT charge on Pd: 0.437) and **4c** (APT charge on Pd: 0.228) support the interpretation of increased covalency. These calculations also corroborate an increased stability of the *P*,*C* coordination for the dimethylamino-functionalised compound (see the Supporting Information).

There may be various reasons for the different behaviour of the –NHR/–NH_2 and the –NR_2 functionalised systems: 1) the NH moiety allows intramolecular hydrogen bonding to one of the chlorido ligands, preventing decoordination of the pyrimidine ligand; 2) the bulky –NR_2 group undergoes repulsive interaction with one of the chlorido ligands, facilitating decoordination of the pyrimidine ligand; or 3) the strongly electron donating –NR_2 group stabilises the C–H activated product more efficiently than a –NHR/–NH_2 group. The latter reason should not play a key role since the calculated APT charges of the carbon atoms in the 5-position of the pyrimidine ring (*trans* to the amino group) for the *P*,*N*-coordinated compounds **3a** (–0.190) and **4a** (–0.212) do not differ largely. We therefore assigned the favoured C–H activation of the –NR_2 functionalised systems to a destabilisation of the *P*,*N*-coordination due to steric reasons and the missing hydrogen bond.

Suzuki–Miyaura Coupling

The palladium(II) complexes **3a**,**b** and **4c**–**e**, were investigated as catalysts for the Suzuki–Miyaura coupling reaction. To optimise the reaction conditions, we initially examined the coupling reaction of bromobenzene and phenylboronic acid with **3a** at 70 °C (Table S1, Supporting Information). The reaction is strongly dependent on the base and the solvent employed. A combination of Cs_2CO_3 and EtOH gave the best results; 93% conversion of bromobenzene was achieved at 70 °C in 45 min with just 0.1 mol-% of **3a** (TOF: 1240 mol·mol^{-1} h^{-1}). We then explored the influence of the amino substituent with catalysts **3a**,**b** and **4c** (Table 1).

Table 1. Coupling reactions of PhBr and $PhB(OH)_2$ with **3a**,**b** and **4c** at variable temperatures.[a]

Entry	Cat.	*T* [°C]	Time [min]	% Conversion[b]
1	**3a**	70	15	49
2	**3b**	70	15	96
3	**4c**	70	15	75
4	**3a**	60	45	traces
5	**3b**	60	45	97
6	**4c**	60	45	83
7	**3a**	40	45	0
8	**3b**	40	45	12
9	**4c**	40	45	90
10	**3a**	r.t.	45	0
11	**3a**	r.t.	240	0
12	**3b**	r.t.	45	traces
13	**3b**	r.t.	240	23
14	**4c**	r.t.	45	46
15	**4c**	r.t.	240	87

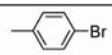
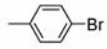
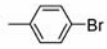
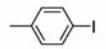
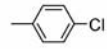
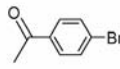
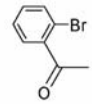
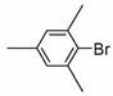
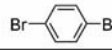
[a] PhBr (1 mmol), $PhB(OH)_2$ (1.2 mmol), Cs_2CO_3 (1.2 mmol), catalyst (0.1 mol-%), EtOH (5 mL). [b] Determined by GC based on PhBr.

Whereas at 70 °C the activities of **3a**,**b** and **4c** differ solely by a factor of two, a decrease in the reaction temperature to 60 °C makes catalyst **3a** fail completely. Going down to even lower temperatures (40 °C) further differentiates between **4c** (90%) and **3b** (12%). Investigations at room temperature showed that **3b** and **4c** are still active; **4c** gave 87% conversion of bromobenzene after 240 min. Encouraged by these results the reaction conditions were reoptimised for **4c**. It was found that the best results were obtained with a 1:1 mixture of DMF/H_2O and Cs_2CO_3 as the base; 0.1 mol-% of the catalyst gave 80% conversion of bromobenzene in 45 min at room temperature.

To elucidate the influence of the amine substituents, the pyrrolidinyl and piperidinyl functionalised catalysts **4d** and **4e** were included in the study. The bulky piperidinyl group gave even better results than **4c** for the coupling of 4-bromotoluene with phenylboronic acid (Table 2, entries 1–3). Whereas 4-iodotoluene underwent coupling with phenylboronic acid (entry 4), the catalyst failed to facilitate the coupling of 4-chlorotoluene with the same acid (entry 5). Reacting 4-bromoacetophenone as an electron deficient substrate gave the coupled product in 93% yield after 1 h with 0.1 mol-% and after 10 h with 0.01 mol-% of catalyst (entries 6 and 7). Sterically hindered substrates bearing one *ortho*-substituent could also be coupled efficiently at room temperature with 0.1 mol-% of catalyst **4e** in just 1 h (entries 9 and 10). However, 2-bromomesitylene bearing two methyl substituents in the *ortho*-position to bromine required a higher catalyst loading (1 mol-%, entry 12). On the other hand, 0.1 mol-% of **4e** resulted in the almost quantitative coupling of 1,4-dibromobenzene with 2.5 equiv. of phenylboronic acid at room temperature in 1 h (entry 13).

We are currently investigating the role of the C–H activation on the catalytic activity of the palladium complexes. In the commonly accepted mechanism of palladium-catalysed coupling reactions, palladium(0) species, either introduced directly or formed in-situ, undergo oxidative addition of the aryl halide. Amatore et al. proved for the Heck olefination and other coupling reactions, that the formation of anionic palladium(0) species such as $[XPdL_2]^-$ (X = halide, acetate, etc.) strongly facilitates the oxidative addition of the substrate.[18] As the basis of our on-going investigations, we assume that, in the presence of a base such as Cs_2CO_3, C–H activation of the pyrimidine site will lead to anionic palladium(II) compounds, which, after in-situ reduction, will give anionic palladium(0) species.

Table 2. Coupling reactions of a variety of aryl halides with phenylboronic acid at room temperature using the palladium catalysts **4c**–**e**.[a]

Entry	Aryl halide	Cat.	Cat. loading (mol-%)	Yield (%)[b]
1		**4c**	0.1	77
2		**4d**	0.1	59
3		**4e**	0.1	88
4		**4e**	0.1	61
5		**4e**	0.1	0
6		**4e**	0.1	93
7[c]			0.01	93
8[c]			0.001	6
9		**4e**	0.1	41
10		**4e**	0.1	8
11		**4e**	0.1	traces
12[c]			1	48
13[d]		**4e**	0.1	95[e]

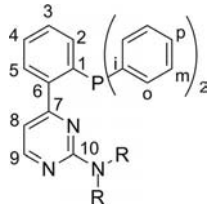
[a] Aryl halide (1 mmol), phenylboronic acid (1.2 mmol), Cs_2CO_3 (1.2 mmol), reaction time: 1 h, DMF/H_2O (v/v = 1:1, 5 mL), room temperature. [b] NMR yield. [c] 10 h. [d] Phenylboronic acid (2.5 mmol). [e] Isolated yield.

Conclusion

In summary, we were able to show that slight changes at the amino group of [(2-aminopyrimidin-4-yl)aryl]phosphanes lead to pronounced differences in the stability and catalytic activity of the corresponding palladium(II) complexes. The ligands we have applied here are accessible on a large scale from versatile starting materials and their general chemical structure can be easily varied; even chiral ligands can be synthesised in just a few steps. Further increasing the electron density at the palladium centre can be achieved by exchanging the diaryl substituent on the phosphanyl group for a dialkyl substituent; this is currently under investigation for the activation of aryl chlorides.

Experimental Section

General: Solvents were purified and dried by standard methods. All reactions were carried out under an atmosphere of dinitrogen. The ligand precursor **1** and the palladium(II) complex $(C_6H_5CN)_2PdCl_2$ were synthesised according to procedures published in the literature.[19,17b] The NMR spectra are assigned according to Scheme 4.



Scheme 4. Numbering scheme for assignment of the NMR signals.

General Synthesis of Ligands 2a-e: 1 (3.0 g, 8.35 mmol) and the appropriate substituted guanidinium sulfate (12 mmol) were suspended in dry EtOH (40 mL). After the addition of KOH (0.67 g), the mixture was heated under reflux for 20 h. After the removal of the solvent in vacuo, the residue was dissolved in a mixture of water and CH_2Cl_2. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (10 mL). The combined organic layers were dried with anhydrous magnesium sulfate, filtered and concentrated in vacuo. The crude material was crystallised from ethanol to afford the desired ligands **2a**–**e** in yields of >90%.

2a: From guanidinium sulfate, yield 2.84 g (96%). $C_{22}H_{18}N_3P$ (355.38): calcd. C 74.35, H 5.11, N 11.82; found C 74.01, H 5.25, N 11.75. ^{1}H NMR ([D$_6$]DMSO, 400.13 MHz): δ = 6.25 (br., 2 H, NH_2), 6.67 (d, $^3J_{HH}$ = 4.8 Hz, 1 H, 8-H), 6.98 (m, 1 H, 2-H), 7.12–7.23 (m, 4 H, *m*-H), 7.30–7.36 (m, 6 H, *o*-H, *p*-H), 7.38 (t, $^3J_{HH}$ = 7.8 Hz, 1 H, 3-H), 7.47 (t, $^3J_{HH}$ = 7.3 Hz, 1 H, 4-H), 7.63 (m, 1 H, 5-H), 8.16 (d, 1 H, 9-H) ppm. ^{13}C NMR ([D$_6$]DMSO, 100.61 MHz): δ = 109.7 (d, $^4J_{CP}$ = 4.6 Hz, C-8), 128.6 (s, C-*m*), 128.6 (s, C-*p*), 128.8 (d, $^3J_{CP}$ = 28.5 Hz, C-2), 129.2 (br., C-3, C-4), 133.2 (d, $^2J_{CP}$ = 20.4 Hz, C-*o*), 134.3 (s, C-5), 135.4 (d, $^1J_{CP}$ = 20.4 Hz, C-1), 138.0 (d, $^1J_{CP}$ = 11.1 Hz, C-*i*), 143.6 (d, $^2J_{CP}$ = 24.0 Hz, C-6), 157.8 (s, C-9), 162.6 (s, C-10), 165.8 (d, $^3J_{CP}$ = 2.8 Hz, C-7) ppm. ^{31}P NMR ([D$_6$]DMSO, 161.98 MHz): δ = –12.05 (s) ppm.

2b: From *N*-ethylguanidinium sulfate, yield 3.01 g (94%). $C_{24}H_{22}N_3P$ (383.43): calcd. C 75.18, H 5.78, N 10.95; found C 74.61, H 5.82, N 10.80. ^{1}H NMR ([D$_6$]DMSO, 400.13 MHz): δ = 0.82 (br., 3 H, NCH_2CH_3), 2.75 (br., 2 H, NCH_2CH_3), signal not observed: NH, δ = 6.68 (br., 1 H, 8-H), 6.98 (m, 1 H, 2-H), 7.12–7.23 (m, 4 H, *m*-H), 7.30–7.36 (m, 6 H, *o*-H, *p*-H), 7.39 (t, $^3J_{HH}$ = 7.8 Hz, 1 H, 3-H), 7.49 (t, $^3J_{HH}$ = 7.4 Hz, 1 H, 4-H), 7.61 (m, 1 H, 5-H$_{pyrim}$), 8.21 (d, $^3J_{HH}$ = 5.1 Hz, 1 H, 9-H) ppm. ^{13}C NMR ([D$_6$]-DMSO, 100.61 MHz): δ = 14.8 (s, NCH_2CH_3), 34.92 (s, NCH_2CH_3), 109.0 (s, C-8), 128.4 (s, C-*m*), 128.5 (s, C-*p*), 128.8 (d, $^3J_{CP}$ = 16.6 Hz, C-2), 129.2, 129.3 (2× s, C-3, C-4), 133.2 (d, $^2J_{CP}$ = 20.3 Hz, C-*o*), 134.7 (s, C-5), 135.3 (d, $^1J_{CP}$ = 19.6 Hz, C-1), 138.2 (d, $^1J_{CP}$ = 12.0 Hz, C-*i*), 144.5 (br., C-6), 157.9 (s, C-9), 161.5 (s, C-10), 166.2 (s, C-7) ppm. ^{31}P NMR ([D$_6$]DMSO, 161.98 MHz): δ = –12.05 (s) ppm.

2c: From *N*,*N*-dimethylguanidinium sulfate, yield 2.98 g (93%). $C_{24}H_{22}N_3P$ (383.43): calcd. C 75.18, H 5.78, N 10.95; found C 75.20, H 5.88, N 10.93. ^{1}H NMR ([D$_6$]DMSO, 400.13 MHz): δ = 2.80 [br., 6 H, $N(CH_3)_2$], 6.71 (d, $^3J_{HH}$ = 4.7 Hz, 1 H, 8-H), 6.98 (m, 1 H, 2-H), 7.10–7.21 (m, 4 H, *m*-H), 7.22–7.35 (m, 6 H, *o*-H, *p*-H), 7.38 (t, $^3J_{HH}$ = 7.8 Hz, 1 H, 3-H), 7.48 (t, $^3J_{HH}$ = 7.4 Hz, 1 H, 4-H), 7.61 (m, 5-H), 8.31 (d, 1 H, 9-H) ppm. ^{13}C NMR ([D$_6$]-DMSO, 100.61 MHz): δ = 36.3 [s, $N(CH_3)_2$], 108.4 (s, C-8), 128.4, 128.4 (2× s, C-*m*, C-*p*), 129.1 (d, $^3J_{CP}$ = 12.8 Hz, C-2), 129.3, 129.3 (2× s, C-3, C-4), 133.2 (d, $^2J_{CP}$ = 19.4 Hz, 4 C, C-*o*), 134.7 (s, C-5), 135.3 (d, $^1J_{CP}$ = 19.4 Hz, C-1), 138.2 (d, $^1J_{CP}$ = 12.9 Hz, C-*i*), 144.6 (d, $^2J_{CP}$ = 24.0 Hz, C-6), 157.8 (s, C-9), 161.1 (s, C-10), 166.4 (s, C-7) ppm. ^{31}P NMR ([D$_6$]DMSO, 161.98 MHz): δ = –12.04 (s) ppm.

2d: From pyrrolidinylguanidinium sulfate, yield 3.12 g (91%). $C_{26}H_{24}N_3P$ (409.47): calcd. C 76.27, H 5.91, N 10.26; found C 76.11, H 5.99, N 10.20. ^{1}H NMR ([D$_6$]DMSO, 400.13 MHz): δ = 1.55–1.80 [br., 4 H, $N(CH_2CH_2)_2$], 2.81 [br., 2 H, $N(CH_2CH_2)_2$], 3.36 [br., 2 H, $N(CH_2CH_2)_2$], 6.73 (d, $^3J_{HH}$ = 5.1 Hz, 1 H, 8-H), 6.97 (m, 1 H, 2-H), 7.12–7.20 (m, 4 H, *m*-H), 7.30–7.36 (m, 6 H, *o*-H, *p*-H), 7.39 (t, $^3J_{HH}$ = 7.4 Hz, 1 H, 3-H), 7.49 (t, $^3J_{HH}$ = 7.4 Hz, 1 H, 4-H), 7.63 (m, 1 H, 5-H), 8.31 (d, 1 H, 9-H) ppm. ^{13}C NMR ([D$_6$]-DMSO, 100.61 MHz): δ = 24.8 [s, $N(CH_2CH_2)_2$], 45.7 [br., $N(CH_2CH_2)_2$], 108.3 (s, C-8), 128.3, 128.3 (2× s, C-*m*, C-*p*), 129.0 (d, $^3J_{CP}$ = 13.9 Hz, C-2), 129.2, 129.2 (2× s, C-3, C-4), 133.3 (d, $^2J_{CP}$ = 19.4 Hz, C-*o*), 134.8 (s, C-5), 135.3 (d, $^1J_{CP}$ = 20.3 Hz, C-1), 138.4 (d, $^1J_{CP}$ = 13.0 Hz, C-*i*), 144.7 (d, $^2J_{CP}$ = 24.0 Hz, C-6), 157.8 (s, C-9), 159.3 (s, C-10), 166.3 (d, $^3J_{CP}$ = 1.9 Hz, C-7) ppm. ^{31}P NMR ([D$_6$]DMSO, 161.98 MHz): δ = –12.08 (s) ppm.

2e: From piperidinylguanidinium sulfate, yield 3.11 g (90%). $C_{27}H_{26}N_3P$ (423.50): calcd. C 76.58, H 6.19, N 9.92; found C 76.53, H 6.30, N 9.80. ^{1}H NMR ([D$_6$]DMSO, 400.13 MHz): δ = 1.26 [br., 4 H, $N(CH_2CH_2)_2CH_2$], 1.47 [br., 2 H, $N(CH_2CH_2)_2CH_2$], 3.34 [br., 4 H, $N(CH_2CH_2)_2CH_2$], 6.75 (d, $^3J_{HH}$ = 5.1 Hz, 1 H, 8-H), 6.99 (m, 1 H, 2-H), 7.13–7.16 (m, 4 H, *m*-H), 7.20–7.35 (m, 6 H, *o*-H, *p*-H), 7.39 (t, $^3J_{HH}$ = 7.8 Hz, 1 H, 3-H), 7.49 (t, $^3J_{HH}$ = 7.4 Hz, 1 H, 4-H), 7.62 (m, 1 H, 5-H), 8.33 (d, 1 H, 9-H) ppm. ^{13}C NMR ([D$_6$]DMSO, 100.61 MHz): δ = 24.2 [s, $N(CH_2CH_2)_2CH_2$], 25.5 [s, $N(CH_2CH_2)_2CH_2$], 43.9 [s, $N(CH_2CH_2)_2CH_2$], 108.5 (s, C-8), 128.4, 128.4 (2× s, C-*m*, C-*p*), 129.2 (d, $^3J_{CP}$ = 17.5 Hz, C-2), 129.3, 129.4 (2× s, C-3, C-4), 133.2 (d, $^2J_{CP}$ = 19.4 Hz, C-*o*), 134.9 (s, C-2), 135.3 (d, $^1J_{CP}$ = 19.4 Hz, C-1), 138.4 (d, $^1J_{CP}$ = 12.9 Hz, C-*i*), 144.6 (d, $^2J_{CP}$ = 24.0 Hz, C-6), 158.0 (s, C-9), 160.3 (s, C-10), 166.5 (d, $^3J_{CP}$ = 1.9 Hz, C-7) ppm. ^{31}P NMR ([D$_6$]DMSO, 161.98 MHz): δ = –12.22 (s) ppm.

General Synthesis of the Palladium Complexes: 3a,b and **4c**–**e** were obtained by treating $(C_6H_5CN)_2PdCl_2$ with ligands **2a**–**e** in equimolar amounts according to the following general method: A solution of the appropriate ligand **2a**–**e** (0.30 mmol) in CH_2Cl_2 (5 mL) was added to a solution of $[(C_6H_5CN)_2PdCl_2]$ (0.115 g, 0.30 mmol) in CH_2Cl_2 (20 mL). The mixture was stirred for 16 h at room temperature. Addition of diethyl ether (50 mL) caused precipitation of the product, which was further washed two times with diethyl ether (20 mL) and dried in the vacuum giving yields of 80–95%.

3a: From **2a**, yield 0.149 g (93%). $C_{22}H_{18}Cl_2N_3PPd$ (532.68): calcd. C 49.60, H 3.41, N 7.89; found C 49.35, H 3.62, N 7.80. ^{1}H NMR ([D$_6$]DMSO, 400.13 MHz): not det. NH_2, δ = 6.89 (d, $^3J_{HH}$ = 4.7 Hz, 1 H, 8-H), 7.18 (m, 2 H, 2-H), 7.23–7.68 (m, 10 H, *o*-H, *m*-H, *p*-H), 7.78 (t, $^3J_{HH}$ = 7.8 Hz, 1 H, 3-H), 7.91 (t, $^3J_{HH}$ = 7.8 Hz, 1 H, 4-H), 8.09 (m, 1 H, 5-H), 8.23 (d, 1 H, 9-H) ppm. ^{31}P NMR ([D$_6$]DMSO, 161.98 MHz): δ = 31.27 (s) ppm.

3b: From **2b**, yield 0.151 g (90%). $C_{24}H_{22}Cl_2N_3PPd$ (560.74): calcd. C 51.41, H 3.95, N 7.49; found C 51.07, H 3.93, N 7.33. ^{1}H NMR ([D$_6$]DMSO, 400.13 MHz): δ = 1.13 (t, $^3J_{HH}$ = 7.0 Hz, 3 H, NCH_2CH_3), 3.51 (br., 2 H, NCH_2CH_3), 6.87 (d, $^3J_{HH}$ = 5.1 Hz, 1 H, 8-H), 7.19 (m, 1 H, 2-H), 7.25–7.72 (m, 10 H, *o*-H, *m*-H, *p*-H), 7.78 (t, $^3J_{HH}$ = 7.8 Hz, 1 H, 3-H), 7.91 (t, $^3J_{HH}$ = 7.8 Hz, 1 H, 4-

Table 3. Summary of the crystallographic data and details of data collection and refinement.

	2a	**2e**	**3a**	**4c**
Empirical formula	$C_{22}H_{18}N_3P$	$C_{27}H_{26}N_3P$	$C_{22}H_{18}Cl_2N_3PPd$	$C_{24}H_{22}Cl_2N_3PPd$
Formula weight	355.36	423.48	532.66	560.72
Crystal size [mm]	$0.28 \times 0.18 \times 0.16$	$0.25 \times 0.21 \times 0.18$	$0.22 \times 0.09 \times 0.09$	$0.10 \times 0.04 \times 0.03$
T [K]	150(2)	150(2)	150(2)	150(2)
λ [Å]	1.54184	1.54184	1.54184	1.54184
Crystal system	triclinic	monoclinic	monoclinic	monoclinic
Space group	$P\bar{1}$	$P2_1/n$	$P2_1/n$	$P2_1/n$
a [Å]	7.6009(2)	10.7084(2)	10.37080(10)	9.6797(1)
b [Å]	7.8075(3)	8.8315(1)	14.7430(2)	16.7909(2)
c [Å]	48.9141(10)	23.3496(4)	13.7009(2)	16.9032(3)
α [°]	89.235(2)	90	90	90
β [°]	89.139(2)	90.199(2)	90.4240(10)	95.074(1)
γ [°]	69.160(3)	90	90	90
V [Å^3]	2712.45(14)	2208.19(6)	2094.77(5)	2736.53(6)
Z	6	4	4	4
$\rho_{calcd.}$ [g cm^{-3}]	1.305	1.274	1.689	1.361
μ [mm^{-1}]	1.413	1.240	10.325	7.930
θ range [°]	3.62–62.61	3.79–62.72	4.41–62.60	3.72–62.62
Reflections collected	24323	14940	14832	20197
Independent reflections	8464	3521	3342	4376
R_{int}	0.0209	0.0193	0.0244	0.0692
Data / restr. / param.	8464 / 342 / 831	3521 / 0 / 280	3342 / 2 / 268	4376 / 1 / 285
Final R indices [$I > 2\sigma(I)$][a]	0.0341, 0.0922	0.0336, 0.0877	0.0215, 0.0558	0.0330, 0.0870
R Indices (all data)	0.0386, 0.0943	0.0361, 0.0888	0.0232, 0.0565	0.0388, 0.0887
GooF[b]	1.066	1.104	1.076	0.969
$\Delta\rho_{max.}$ / $_{min.}$ [e Å^{-3}]	0.258 / –0.648	0.320 / –0.291	0.536 / –0.459	0.446 / –0.703

[a] $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$, $\omega R_2 = [\Sigma\omega(F_o^2 - F_c^2)^2/\Sigma\omega F_o^2]^{1/2}$. [b] $GooF = [\Sigma\omega(F_o^2 - F_c^2)^2/(n - p)]^{1/2}$.

H), 8.11 (m, 1 H, 5-H_{pyrim}), 8.29 (d, 1 H, 9-H), 8.50 (br., 1 H, NH) ppm. ^{31}P NMR ([D$_6$]DMSO, 161.98 MHz): δ = 30.71 (s) ppm.

4c: From **2c**, yield 0.147 g (87%). $C_{24}H_{22}Cl_2N_3PPd$ (560.74): calcd. C 51.41, H 3.95, N 7.49; found C 52.98, H 3.98, N 7.78. ^{1}H NMR ([D$_6$]DMSO, 400.13 MHz): not det. NH, δ = 3.14 [s, 6 H, N-$(CH_3)_2$], 6.84 (br., 1 H, 2-H), 7.30–7.50 (m, 10 H, *o*-H, *m*-H, *p*-H), 7.59 (m, 1 H, 3-H), 7.75 (t, $^3J_{HH}$ = 7.0 Hz, 1 H, 4-H), 8.45 (m, 1 H, 5-H), 8.52 (s, 1 H, 9-H) ppm. ^{31}P NMR ([D$_6$]DMSO, 161.98 MHz): δ = 29.69 (s) ppm.

4d: From **2d**, yield 0.149 g (85%). $C_{26}H_{24}Cl_2N_3PPd$ (586.78): calcd. C 53.22, H 4.12, N 7.16; found C 53.47, H 4.11, N 7.16. ^{1}H NMR ([D$_6$]DMSO, 400.13 MHz): δ = not det. NH, 1.93 [br., 4 H, $N(CH_2CH_2)_2$], 3.51 [br., 4 H, $N(CH_2CH_2)_2$], 6.84 (br., 1 H, 2-H), 7.30–7.50 (m, 10 H, *o*-H, *m*-H, *p*-H), 7.58 (m, 1 H, 3-H), 7.75 (t, $^3J_{HH}$ = 7.9 Hz, 1 H, 4-H), 8.45 (m, 1 H, 5-H), 8.51 (s, 1 H, 9-H) ppm. ^{31}P NMR ([D$_6$]DMSO, 161.98 MHz): δ = 29.67 (s) ppm.

4e: From **2e**, yield 0.150 g (83%). $C_{27}H_{26}Cl_2N_3PPd\cdot(CH_2Cl_2)_{0.67}$: calcd. C 50.54, H 4.19, N 6.53; found C 50.79, H 4.14, N 6.40. ^{1}H NMR ([D$_6$]DMSO, 400.13 MHz): δ = not det. NH, 1.59 [br., 6 H, $N(CH_2CH_2)_2CH_2$], 3.68 [br., 4 H, $N(CH_2CH_2)_2CH_2$], 6.84 (br., 1 H, 2-H), 7.32–7.42 (m, 4 H, *o*-H), 7.44–7.54 (m, 6 H, *m*-H, *p*-H), 7.58 (m, 3-H_{pyrim}), 7.75 (t, $^3J_{HH}$ = 7.4 Hz, 1 H, 4-H), 8.40 (m, 5-H), 8.52 (s, 1 H, 9-H) ppm. ^{31}P NMR ([D$_6$]DMSO, 161.98 MHz): δ = 29.60 (s) ppm.

X-ray Structure Analyses: Crystal data and refinement parameters for compounds **2a**, **2e**, **3a** and **4c** are collected in Table 3. The structures were solved by direct methods (SIR92[20]), completed by subsequent difference Fourier syntheses, and refined by full-matrix least-squares procedures.[21] Semi-empirical absorption corrections from equivalents (Multiscan) were carried out.[22] All non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms, which are bound to the nitrogen atoms, were located in the difference Fourier synthesis and were refined semi-freely with the help of a distance restraint while constraining their U values to 1.2 times the U_{eq} value of the attached nitrogen atoms. All the other hydrogen atoms were placed in calculated positions and refined by using a riding model. For compound **4c**, because of the existence of severely disordered solvents (probably the mixture of pentane, CH_2Cl_2/$CHCl_3$ and/or H_2O), the SQUEEZE process integrated in PLATON has been used.

CCDC-831761 (for **2a**), -831763 (for **2e**), -831762 (for **3a**) and -831764 (for **4c**) 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.

DFT Calculations: Quantum chemical calculations on the compounds **3a**,**c** and **4a**,**c** were performed with the program Gaussian 03W[23] using the B3LYP gradient corrected exchange-correlation functional[24] in combination with the 6-31G* basis set[25] for C, H, N, P, Cl and the LANL2DZ (ECP) basis set for Pd.[26] Full geometry optimisations were carried out in C_1 symmetry using analytical gradient techniques and the resulting structures were confirmed to be true minima by diagonalisation of the analytical Hessian Matrix.

Supporting Information (see footnote on the first page of this article): Tables and figures giving X-ray structure data, NMR and IR spectra.

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[1] X.-F. Wu, P. Anbarasan, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2010**, *49*, 9047–9050.

[2] a) R. F. Heck, *Acc. Chem. Res.* **1979**, *12*, 146–151; b) I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009–3066; c) E. Negishi, C. Copéret, S. Ma, S.-Y. Liou, F. Liu, *Chem. Rev.* **1996**, *96*, 365–394.

[3] a) E. Negishi, A. O. King, N. Okukado, *J. Org. Chem.* **1977**, *42*, 1821; b) E. Negishi, *Acc. Chem. Res.* **1982**, *15*, 340–348; c) E. Negishi, L. Anastasia, *Chem. Rev.* **2003**, *103*, 1979–2018.

[4] a) N. Miyaura, K. Yamada, A. Suzuki, *Tetrahedron Lett.* **1979**, *20*, 3437–3440; b) N. Miyaura, A. Suzuki, *J. Chem. Soc., Chem. Commun.* **1979**, 866–867; c) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457–3483.

[5] a) A. F. Littke, G. C. Fu, *Angew. Chem. Int. Ed.* **2002**, *41*, 4176–4211; b) A. Zapf, R. Jackstell, F. Rataboul, T. Riermeier, A. Monsees, C. Fuhrmann, N. Shaikh, U. Dingerdissen, M. Beller, *Chem. Commun.* **2004**, 38–39.

[6] a) A. Zapf, A. Ehrentraut, M. Beller, *Angew. Chem.* **2000**, *112*, 4315–4317; *Angew. Chem. Int. Ed.* **2000**, *39*, 4153–4155; b) R. B. Bedford, C. S. J. Cazin, S. L. Hazelwood, *Angew. Chem. Int. Ed.* **2002**, *41*, 4120–4122; c) R. B. Bedford, S. L. Hazelwood, M. E. Limmert, *Chem. Commun.* **2002**, 2610–2611; d) R. B. Bedford, S. L. Hazelwood, M. E. Limmert, D. A. Albisson, S. M. Draper, P. N. Scully, S. J. Coles, M. B. Hursthouse, *Chem. Eur. J.* **2003**, *9*, 3216–3227; e) B. Karimi, P. F. Akhavan, *Chem. Commun.* **2009**, 3750–3752.

[7] a) J. Yin, M. P. Rainka, X.-X. Zhang, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 1162–1163; b) G. Altenhoff, R. Goddard, C. W. Lehmann, F. Glorius, *J. Am. Chem. Soc.* **2004**, *126*, 15195–15201; c) A. Schmidt, A. Rahimi, *Chem. Commun.* **2010**, *46*, 2995–2997.

[8] Some recent references for phosphane ligands applied in C-C cross-coupling reactions: a) M. J. Burns, I. J. S. Fairlamb, A. R. Kapdi, P. Sehnal, R. J. K. Taylor, *Org. Lett.* **2007**, *9*, 5397–5400; b) A. S. Guram, X. Wang, E. E. Bunel, M. M. Faul, R. D. Larsen, M. J. Martinelli, *J. Org. Chem.* **2007**, *72*, 5104–5112; c) K. Billingsley, S. L. Buchwald, *J. Am. Chem. Soc.* **2007**, *129*, 3358–3366; d) C. A. Fleckenstein, H. Plenio, *Green Chem.* **2007**, *9*, 1287–1291; e) A. T. Lindhardt, M. L. H. Mantel, T. Skrydstrup, *Angew. Chem.* **2008**, *120*, 2708–2712; *Angew. Chem. Int. Ed.* **2008**, *47*, 2668–2672; f) B. H. Lipshutz, B. R. Taft, *Org. Lett.* **2008**, *10*, 1329–1332.

[9] D. W. Old, J. P. Wolfe, S. L. Buchwald, *J. Am. Chem. Soc.* **1998**, *120*, 9722–9723.

[10] S. Vyskocil, M. Smrcina, V. Hanus, M. Polasek, P. Kocvsky, *J. Org. Chem.* **1998**, *63*, 7738–7748.

[11] P. Koovsky, S. Vyskocil, I. Cisarova, J. Sejbal, I. Tislerova, M. Smrina, G. C. Lloyd-Jones, S. C. Stephen, C. P. Butts, M. Murray, V. Langer, *J. Am. Chem. Soc.* **1999**, *121*, 7714–7715.

[12] J. Yin, S. L. Buchwald, *J. Am. Chem. Soc.* **2000**, *122*, 12051–12052.

[13] J. W. Faller, N. Sarantopoulos, *Organometallics* **2004**, *23*, 2008–2014.

[14] U. Christmann, D. A. Pantazis, J. Benet-Buchholz, J. E. McGrady, F. Maseras, R. Vilar, *J. Am. Chem. Soc.* **2006**, *128*, 6376–6390.

[15] R. Paratap, D. Parrish, P. Gunda, D. Venkataraman, M. K. Lakshman, *J. Am. Chem. Soc.* **2009**, *131*, 12240–12249.

[16] a) W. R. Thiel, T. Priermeier, *Angew. Chem.* **1995**, *107*, 1870–1872; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1737–1738; b) W. R. Thiel, J. Eppinger, *Chem. Eur. J.* **1997**, *3*, 696–705; c) H. Glas, M. Barz, W. R. Thiel, *J. Organomet. Chem.* **2001**, *621*, 153–157; d) M. Jia, W. R. Thiel, *Chem. Commun.* **2002**, 2392–2393; e) Y. Sun, A. Hienzsch, J. Grasser, E. Herdtweck, W. R. Thiel, *J. Organomet. Chem.* **2006**, *691*, 291–298; f) D. Zabel, A. Schubert, G. Wolmershäuser, R. L. Jones Jr., W. R. Thiel, *Eur. J. Inorg. Chem.* **2008**, 3648–3654; g) T. Jozak, D. Zabel, A. Schubert, Y. Sun, W. R. Thiel, *Eur. J. Inorg. Chem.* **2010**, *32*, 5135–5145.

[17] a) A. Hienzsch, Y. Sun, W. R. Thiel, WO002006045272; b) A. Reis, W. R. Thiel, DE 102008039167; c) A. Reis, D. Dehe, S. Farsadpour, I. Munstein, Y. Sun, W. R. Thiel, *New J. Chem.*, accepted.

[18] C. Amatore, A. Jutand, *Acc. Chem. Res.* **2000**, *33*, 314–321.

[19] S. Komiya, *Synthesis of organometallic compounds: a practical guide*, John Wiley & Sons, Chichester, **1997**.

[20] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, M. Camalli, *J. Appl. Crystallogr.* **1994**, *27*, 435–435.

[21] G. M. Sheldrick, *Acta Crystallogr., Sect. A* **2008**, *64*, 112–122.

[22] CrysAlisPro, Oxford Diffraction Ltd., version 1.171.33.48, **2009** and version 1.171.33.*66*, **2010**.

[23] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, *Gaussian 03*, revision E.01, Gaussian, Inc., Wallingford CT, **2004**.

[24] a) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789; b) A. D. Becke, *Phys. Rev.* **1988**, *A38*, 3098–3100; c) B. Miehlich, A. Savin, H. Stoll, H. Preuss, *Chem. Phys. Lett.* **1989**, *157*, 200–206.

[25] a) P. C. Hariharan, J. A. Pople, *Theoret. Chim. Acta* **1973**, *28*, 213–222; b) M. M. Francl, W. J. Petro, W. J. Hehre, J. S. Binkley, M. S. Gordon, D. J. DeFrees, J. A. Pople, *J. Chem. Phys.* **1982**, *77*, 3654–3665.

[26] P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 270–283.

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