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Mendeleev Commun., 2007, **17**, 142–144
Mendeleev Communications

Arylamidate palladium complexes containing deprotonated phthalimide and *p*-methylbenzamide: possibility of their participation in reductive elimination

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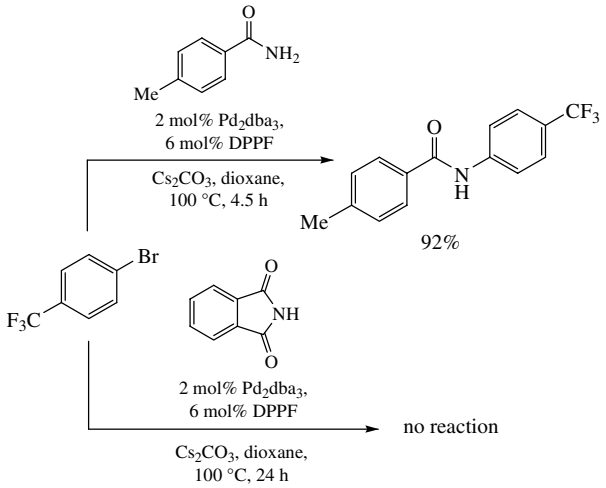
DOI: 10.1016/j.mencom.2007.05.003

Arylamidate palladium complexes containing deprotonated *p*-methylbenzamide and phthalimide have been synthesised; the latter has been characterised by X-ray diffraction data. A comparison of the catalytic and stoichiometric versions of N-arylation of *p*-methylbenzamide and phthalimide in the presence of palladium complexes and DPPF as a ligand has been carried out.

The steps of oxidative addition, transmetallation and migratory insertion are the most important steps of the catalytic cycle determining the overall reaction rate and the very possibility of reactions catalysed by palladium complexes such as cross-coupling, Mizoroki–Heck reaction and many others. The amination of aryl halides (Buchwald–Hartwig reaction)[1] is an exception: the final step, *viz.*, the reductive elimination of arylamines from arylamide palladium complexes, plays a key role in this process. The importance of this step should increase even more for the arylation of amides because the coordinated amide fragment should be less able to reduce palladium(II). Furthermore, the lower nucleophilicity of amides in comparison with amines can slow down the step of halogen substitution by an amide fragment. In fact, the arylation of amides occurs less readily than that of amines, whereas the arylation of low-basic amides seems problematic so far.[2–6]

In this study, we compared the catalytic and stoichiometric arylation of two amides with different basicity, namely, phthalimide and *p*-methylbenzamide. The catalytic version of the reaction was carried out in the presence of 2 mol% Pd_2dba_3, 6 mol% DPPF and Cs_2CO_3 as a base in dioxane at 100 °C. The arylation of *p*-methylbenzamide gives an arylation product in 92% yield, but phthalimide does not react under these conditions (Scheme 1).



Scheme 1

According to the generally accepted mechanism, the amination (amidation) catalytic cycle involves three steps: oxidative addition, substitution of halogen with amine and reductive elimination to give a C–N bond.[7] The oxidative addition of aryl halides to palladium(0) has been studied fairly well for complexes with various ligands.[8–15]

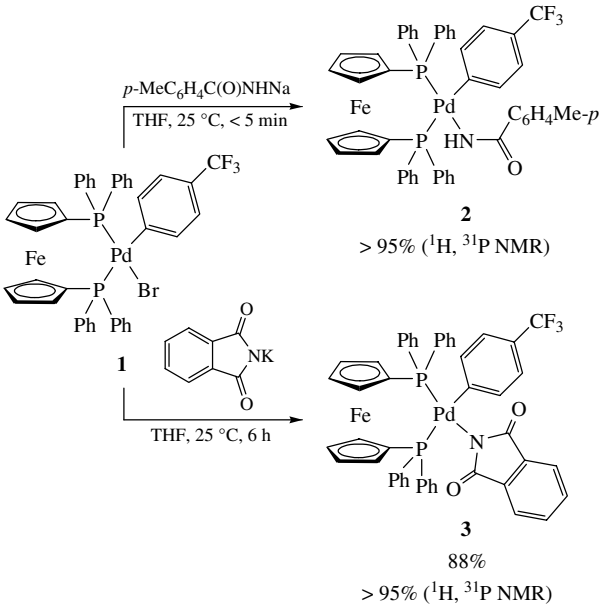
Oxidative addition of *p*-bromobenzotrifluoride to Pd(0) in the presence of DPPF occurs smoothly in toluene at 100 °C to give the Pd(DPPF)(*p*-$C_6H_4CF_3$)Br complex **1** in 83% yield (see Online Supplementary Materials).

$$Pd(dba)_2 + DPPF + p\text{-}CF_3C_6H_4Br \xrightarrow[100\ ^\circ C,\ 1\ h]{toluene} \underset{\mathbf{1}\ 83\%}{Pd(DPPF)(p\text{-}C_6H_4CF_3)Br}$$

In order to obtain arylamide complexes **2** and **3**, we carried out the reactions of complex **1** and N-metallated amides in THF.[†] The reactions occur at room temperature to give arylamide complexes **2** and **3** in quantitative yields (according to ^1H and ^{31}P NMR data). Experiments carried out under the same conditions showed that aryl bromide complex **1** did not react with free amides.

The rate of substitution strongly depends on the nucleophilicity of the anion: the reaction with the sodium salt of *p*-methylbenzamide was completed in less than 5 min, whereas the complete conversion of complex **1** with weakly nucleophilic potassium phthalimide was observed only after 6 h. In ^{31}P NMR spectra, the signals of the original complex at δ 10.4 and 30.4 ($^2J_{PP}$ 32.5 Hz) disappeared and two new doublets appeared at δ 15.2 and 27.7 ($^2J_{PP}$ 30 Hz) for complex **2** and at δ 16.6 and 24.0 ($^2J_{PP}$ 30 Hz) for complex **3**. In the ^1H NMR spectra of amide complexes, the signals of aromatic protons of coordinated amides are shifted upfield with respect to the signals of free amides. The proton signals of coordinated amide in complex **2** are observed at δ 6.72 (d) and 6.95 (d) ($^3J_{HH}$ 8 Hz), those of free amide appear at δ 7.14 (d) and 7.71 (d) ($^3J_{HH}$ 8 Hz), and those in complex **3** appear at δ 7.00–7.15 (m) and 7.65–7.80 (m), respectively. In

[†] During the preparation of this paper, a similar paper was published, which dealt with a synthesis of palladium complexes containing coordinated secondary amides.[16]

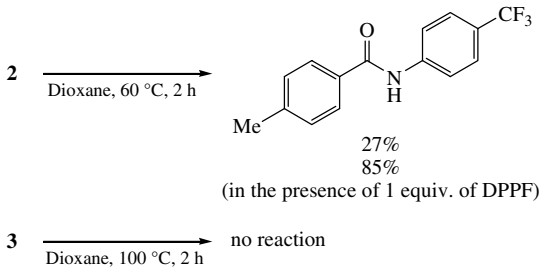


Scheme 2

both cases, amidate complexes are formed irreversibly even in the reaction with the low-basic phthalimide anion.

Phthalimide complex **3** was isolated in 88% yield.‡ Slow diffusion of light petroleum into a chloroform solution of complex **3** gave crystals suitable for X-ray analysis§ in the form of the solvate $\mathbf{3}\cdot 1/2CHCl_3\cdot 3/4C_6H_{14}\cdot 1/2C_7H_{16}$. A unit cell of the complex contains two independent molecules, which have similar bond lengths and bond angles but differ in the DPPF conformation with respect to the aryl and amide ligands. Figure 1 demonstrates the structures of both molecules (**A** and **B**). Complex **3** has a square-planar configuration. The aryl and phthalimide ligands are almost orthogonal to the palladium square plane.

We studied the reductive elimination of *N*-arylamides from the complexes obtained. The heating of complex **2** at 60 °C results in a product in a low yield (27%). However, the addition of 1 equiv. of DPPF allowed us to increase the yield to 85%, *i.e.*, to obtain the product in a yield approaching that of the catalytic reaction. This effect of phosphine addition is difficult to explain. It can be assumed that it is due to the reversibility of the reaction and the ability of 'PdDPPF' to be inserted into the Csp^2–N bond (though it seems problematic) and also due to an equilibrium shift to the right upon formation of $Pd(DPPF)_2$. Another explanation, which is also disputable, involves the assumption that the *N*-arylamide is displaced when the phosphine is added since the electrophilicity of palladium in this complex decreases. Note that the heating of complex **2** in the presence of DPPF as the main phosphorus-containing product results in the $Pd(DPPF)_2$ complex, whereas the same reaction carried out



Scheme 3

without any ligand gives a mixture of several complexes. An increase in the yields of products in reductive elimination of arylamines from Pd(DPPF)(Ar)NRR′ complexes due to the addition of triphenylphosphine was noted by Driver and Hartwig.[19] A similar result was also observed in reductive elimination with formation of C–O,[20] C–S[21] and C–C[22] bonds.

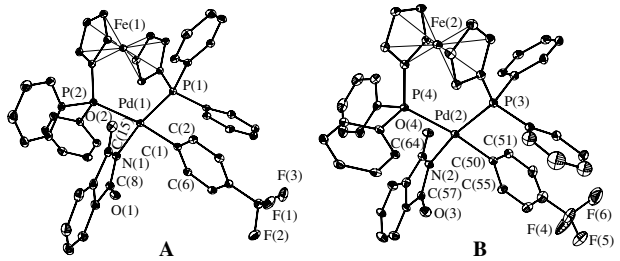


Figure 1 Molecular structure of the $\mathbf{3}\cdot 1/2CHCl_3\cdot 3/4C_6H_{14}\cdot 1/2C_7H_{16}$ complex, where atoms are presented as thermal vibration ellipsoids (the probability is 40%). Two independent molecules are shown, differing in the DPPF conformation with respect to the aryl and amide ligands. Selected bond lengths (Å) and bond angles (°) for **A**: Pd(1)–P(1) 2.2715(12), Pd(1)–P(2) 2.3952(12), Pd(1)–N(1) 2.063(4), Pd(1)–C(1) 2.032(4), P(1)–Pd(1)–P(2) 102.10(4), C(1)–Pd(1)–P(1) 86.36(13), C(1)–Pd(1)–N(1) 82.54(16), N(1)–Pd(1)–P(2), 89.07(11), N(1)–Pd(1)–C(1)–C(6) 86.4(4), C(1)–Pd(1)–N(1)–C(15) 89.3(4); for **B**: Pd(2)–P(3) 2.3007(13), Pd(2)–P(4) 2.3778(13), Pd(2)–N(2) 2.078(4), Pd(2)–C(50) 2.035(5), P(3)–Pd(2)–P(4) 102.15(4), C(50)–Pd(2)–P(3) 85.36(13), C(50)–Pd(2)–N(2) 84.43(17), N(2)–Pd(2)–P(4) 88.08(11), N(2)–Pd(2)–C(50)–C(51) 87.0(4), C(50)–Pd(2)–N(2)–C(57) 75.2(4).

‡ *Complex* **3**. Pd(DPPF)(*p*-$C_6H_4CF_3$)Br (45 mg, 50.8 mmol), potassium phthalimide (11 mg, 59.38 mmol) and THF (2 ml) were placed in a reactor filled with argon. The solution was stirred for 6 h at room temperature, diluted with THF (5 ml), filtered, concentrated to 2 ml and precipitated with light petroleum to give 43 mg of the product as orange-yellow crystals (88%). ^{1}H NMR (THF) δ: 7.71–7.79 (m, 4H), 7.56–7.64 (m, 4H), 7.33–7.39 (m, 2H), 7.23–7.29 (dt, 4H, *J* 2.5 and 8.0 Hz), 7.15–7.23 (m, 8H), 7.10–7.15 (m, 2H), 7.00–7.06 (m, 2H), 6.59 (d, 2H, *J* 8 Hz), 4.41–4.45 (m, 4H), 4.35–4.38 (m, 2H), 4.32–4.35 (m, 2H). ^{31}P NMR (THF) δ: 24.00 (d, *J* 30 Hz), 16.58 (d, *J* 30 Hz). ^{13}C NMR ($CDCl_3$) δ: 177.97, 163.77 (d, J_{C-P} 126 Hz), 137.52, 135.69, 134.63 (d, J_{C-P} 12 Hz), 134.31 (d, J_{C-P} 12 Hz), 133.30 (d, J_{C-P} 37 Hz), 131.87 (d, J_{C-P} 54 Hz), 130.63, 130.55, 130.35, 128.33 (d, J_{C-P} 10 Hz), 128.23 (d, J_{C-P} 10 Hz), 122.90 (m), 120.36, 75.39 (d, J_{C-P} 4.5 Hz), 75.28 (d, J_{C-P} 4 Hz), 73.51 (d, J_{C-P} 6.5 Hz), 73.09 (d, J_{C-P} 7 Hz). IR (THF, ν/cm^{-1}): 1665 ($\nu_{C=O}$).

§ *Crystallographic data for* $\mathbf{3}\cdot 1/2CHCl_3\cdot 3/4C_6H_{14}\cdot 1/2C_7H_{16}$. Crystals of $C_{57.5}H_{55}Cl_{1.5}F_3FeNO_2P_2Pd$ (M = 1126.39) are monoclinic, space group $P2_1/c$, a = 19.2799(14), b = 17.4190(13) and c = 30.120(2) Å, β = 93.424(2)°, V = 10097.2(13) Å^3, Z = 8, d_{calc} = 1.482 g cm^{-3}, λ(MoKα) = 0.71073 Å, μ(MoKα) = 0.842 mm^{-1}, F(000) = 4620, T = 120(2) K.

Crystallographic data for **4**. Crystals of $C_{41}H_{32}ClF_3FeP_2Pd$ (M = = 841.31) are triclinic, space group $P\bar{1}$, a = 11.0112(10), b = 12.0563(12) and c = 14.2026(13) Å, α = 71.630(2)°, β = 89.028(2)°, γ = 78.472(2)°, V = 1751.1(3) Å^3, Z = 2, d_{calc} = 1.596 g cm^{-3}, λ(MoKα) = 0.71073 Å, μ(MoKα) = 1.141 mm^{-1}, F(000) = 848, T = 120(2) K.

The experimental data were obtained using a Bruker SMART 1K three-circle diffractometer. Corrections for the absorption of X-ray irradiation were made semi-empirically using the SADABS software.[17] The structures were determined by direct methods and refined by a full-matrix least-squares method in an anisotropic approximation for non-hydrogen atoms. The positions of hydrogen atoms were calculated geometrically and refined within the riding model with fixed isotropic temperature parameters. All calculations were carried out using the SHELXTL PLUS software (PC Version 5.10).[18] For **3**: R_1 = 0.0697, wR_2 = 0.1431 for 18544 reflections with $I > 2\sigma(I)$, GOF = 0.999. For **4**: R_1 = 0.043, wR_2 = 0.101 for 8082 reflections with $I > 2\sigma(I)$, GOF = 1.038.

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge *via* www.ccdc.cam.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference numbers 624042 and 624043 for **3** and **4**, respectively. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2007.

Unlike *p*-methylbenzamide complex **2**, phthalimide complex **3** is stable even when heated at 100 °C.

This result allows us to explain the fact that phthalimide does not undergo arylation under catalytic conditions. As one can see from the above examples, the reductive elimination of *N*-arylamides from palladium amidate complexes **2** and **3** is much more sensitive to the basicity of the amide anion than substitution of bromine with an amidate fragment ('transmetallation') and requires much more drastic conditions. The series of relative facility of reductive elimination to give a C–N bond from arylpalladium complexes with deprotonated amines and azoles has been reported by Hartwig.[23] The reaction rate increases with amine basicity: reductive elimination from complexes with aliphatic amines and anilines occurs at room temperature, whereas the reaction with diarylamines and azoles requires more drastic conditions: 70 and 100 °C, respectively.[19,24,25] The reductive elimination of *N*-arylamide from amidate complex **2** with deprotonated *p*-methylbenzamide and from complexes with di(*p*-tolyl)amine occurs under similar conditions (60 and 70 °C).[19,25] This agrees with the fact that the basicity of anions of aromatic acid amides is comparable with that of diarylamine anions. In fact, the pK_a of benzamide in DMSO is 23.5, while that of diphenylamine is 24.9.[26] The absence of reductive elimination from complex **3** is undoubtedly due to the very low basicity of the phthalimide anion (pK_a 8.3).

It is interesting to note that, on heating, the chloroform solvate of phthalimide complex, **3**·1/2$CHCl_3$·3/4C_6H_{14}·1/2C_7H_{16}, gives the aryl chloride complex Pd(DPPF)(*p*-$C_6H_4CF_3$)Cl **4** and phthalimide.[§,¶]

Complex **4** was characterised by X-ray diffraction data[§] (Figure 2). We assume that this process involves the acidic

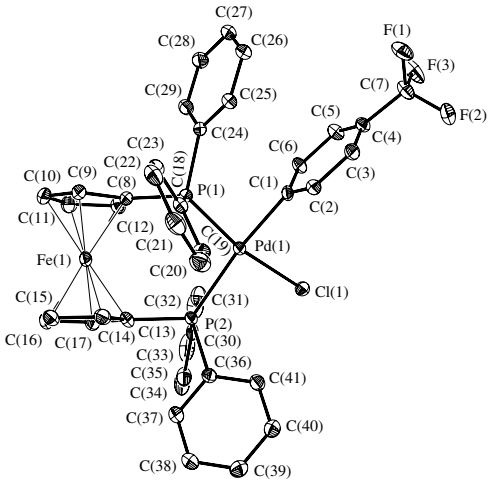
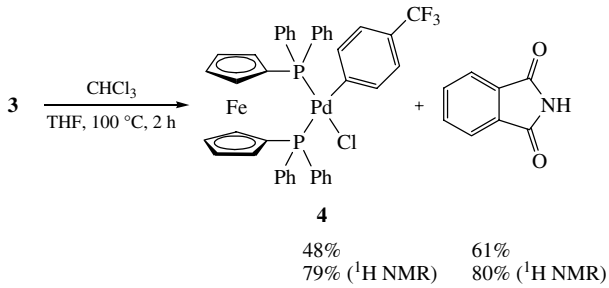


Figure 2 Molecular structure of complex **4**, where atoms are presented as thermal vibration ellipsoids (probability 40%).

¶ A solution of Pd(DPPF)(*p*-$C_6H_4CF_3$)[N{(O)C}·2C_6H_4]·1/2$CHCl_3$·3/4C_6H_{14}·1/2C_7H_{16} (75 mg, 0.0665 mmol) in 2 ml of THF was heated for 2 h in a sealed tube at 100 °C under argon; the reaction mixture was then cooled and concentrated. The residue was chromatographed on 40–63 μm silica gel using a 1:2 ethyl acetate–light petroleum mixture (65–68 °C) as an eluent to give 27 mg (48%) of complex **4** as orange-yellow crystals and 6 mg (61%) of phthalimide. The ^{1}H and ^{31}P NMR spectra of the products obtained are identical to the spectra of the products in the reaction mixture.

Complex **4**. ^{1}H NMR (THF) δ: 8.00–8.13 (m, 4H), 7.37–7.47 (m, 6H), 7.30–7.38 (m, 4H), 7.22–7.30 (m, 2H), 7.00–7.13 (m, 6H), 6.65 (m, quasi-doublet, 2H, *J* 7.5 Hz), 4.76–4.80 (m, 2H), 4.51–4.56 (m, 2H), 4.15–4.20 (m, 2H). ^{1}H NMR ($CDCl_3$) δ: 8.00–8.13 (m, 4H), 7.41–7.52 (m, 6H), 7.27–7.38 (m, 6H), 7.04–7.17 (6H), 6.76 (m, quasi-doublet, 2H, *J* 8 Hz), 4.67–4.73 (m, 2H), 4.48–4.53 (m, 2H), 4.13–4.19 (m, 2H), 3.55–3.62 (m, 2H). ^{31}P NMR (THF) δ: 31.46 (d, *J* 31.5 Hz), 11.09 (d, *J* 31.5 Hz). ^{31}P NMR ($CDCl_3$) δ: 33.25 (d, *J* 32.5 Hz), 12.38 (d, *J* 32.5 Hz).



Scheme 4

cleavage of the C–N bond. The participation of chloroform as an acid in this reaction is unlikely, since the reaction of complex **3** with Bu^{t}OH, which has a similar acidity, does not occur to any noticeable extent under these conditions. Presumably, the cleavage of the complex at the Pd–N bond occurs due to the action of HCl that is formed from chloroform.

Thus, we have synthesised the amidate complexes of palladium with phthalimide and *p*-methylbenzamide ligands and studied the ability of these complexes to participate in reductive elimination resulting in the formation of a C–N bond.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2007.05.003.

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Received: 23rd October 2006; Com. 06/2799