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Palladium-Catalysed Amination Reactions Using Cobalt-Containing Bulky Phosphane Ligands

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Keywords: Amination / Palladium / Cobalt complexes / Phosphane ligands / Orthometallation

Aminations of aryl bromides by morpholine have been investigated using palladium complexes as catalyst precursors modified by the cobalt-containing phosphane ligand $[(\mu\text{-}PPh_2CH_2PPh_2)Co_2(CO)_4][\mu,\eta\text{-}PhC{\equiv}CP(t\mathrm{Bu})_2]$ (**1**). Reactions were carried out under various conditions with satisfactory results. The components of the optimised reaction conditions consist of 1.0 mmol of aryl bromide, 1.2 equiv. of morpholine, 1.4 equiv. of NaO*t*Bu, 1 mL of toluene and 1 mol-% of a 1:1 mixture of **1** and $Pd(OAc)_2$. In contrast, related aminations using $[(\mu\text{-}PPh_2CH_2PPh_2)Co_2(CO)_4][\mu,\eta\text{-}pyC{\equiv}CP(t\mathrm{Bu})_2]$ (**2**), $[(\mu\text{-}PPh_2CH_2PPh_2)Co_2(CO)_4][\{\mu,\eta\text{-}PhC{\equiv}CP(cy)_2\}]$ (**3**) and $[(\mu\text{-}PPh_2CH_2PPh_2)Co_2(CO)_4][\mu,\eta\text{-}PhC{\equiv}CP(i\mathrm{Pr})_2]$ (**4**) as phosphane ligands do not exhibit comparable efficiency. A novel palladium complex **5**, i.e. Pd(OAc) chelated by deprotonated **1** was obtained from the reaction of **1** with $Pd(OAc)_2$. As revealed by the crystal structure, an orthometallation process occurs between the phenyl ring of **1** and the palladium ion. Presumably, the process is accompanied by release of one equivalent of acetic acid. The coordinated acetate ligand binds to the palladium ion in a bidentate chelating mode.

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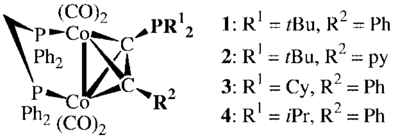
Introduction

The amination of aryl halides by a phosphane-coordinated palladium catalyst is a much more superior method for the preparation of aromatic amines than the original methods using tin amides.[1] Clearly, it is neither ecologically friendly nor practical to use stoichiometric amounts of tin amides in the amination reaction. Recently, momentous improvements have been achieved by Buchwald[2] and Hartwig[3] in the catalytic amination of aryl bromides using free amines. Based on their extensive investigations into this subject, a well accepted mechanism has now been proposed.[4] Recently, a second-generation of much more efficient catalysts for aminations was introduced by Buchwald[5] and Hartwig.[6] These are palladium complexes chelated by biphosphane ligands such as 1,1′-bis(diphenylphosphanyl)ferrocene (dppf) or BINAP. As is known for transition-metal-complex-assisted catalytic reactions, the rate of the reductive elimination process is normally enhanced by employing a bulky ligand such as dppf. Lately, because of their bulky nature, the use of using metal-containing phosphanes in transition-metal catalysed reactions has received increasing attention.[7] In particular, we were interested in exploiting a new type of metal-containing phosphane ligand which would allow us to gain direct access to a family of phosphanes which would hopefully be electron-rich and bulky in character.[7,8] As a result, a new family of novel cobalt-containing (mono- or bidentate) phosphanes has been prepared and their catalytic efficiencies in phosphane modified, palladium-catalysed reactions have been evaluated.[9] It was also found that in most of the phosphane assisted cases, the catalytic efficiencies are higher when using monodentate rather than bidentate phosphanes. Among the monodentate phosphane ligands possible, a series of organometallic versions of tris(alkylphosphanes), $[(\mu\text{-}PPh_2CH_2PPh_2)Co_2(CO)_4][\mu,\eta\text{-}R^2C{\equiv}CPR^1{}_2]$ (**1**: R^1 = *t*Bu, R^2 = Ph; **2**: R^1 = *t*Bu, R^2 = py; **3**:[9a] R^1 = Cy, R^2 = Ph; **4**: R^1 = *i*Pr, R^2 = Ph), were chosen and used in palladium-catalysed amination reactions (Scheme 1). Results of a careful examination of the amination reactions catalysed by $Pd(OAc)_2$ complexes chelated with **1**, **2**, **3** or **4** are reported in this paper. Following this, the efficiencies of these ligands in the reactions are compared and discussed.



Scheme 1.

Results and Discussion

Amination Reactions Using Palladium Complexes Chelated by the Cobalt-Containing Phosphane Ligands 1, 2, 3 and 4

Amination reactions of bromobenzene by morpholine were carried out using palladium complexes chelated by the

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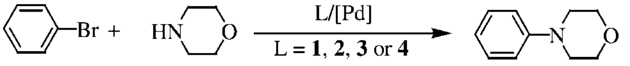
cobalt-containing phosphane ligands **1**, **2**, **3** or **4** as the catalyst precursors (Scheme 2).



Scheme 2.

The general procedure for the catalytic reactions under investigation is as follows. A suitable Schlenk tube was first charged with 1.0 mmol of bromobenzene, 1.2 equiv. of morpholine, 1.4 equiv. of NaO*t*Bu, 1 mL of toluene and 1 mol-% of **1**/Pd(OAc)$_2$. The reaction mixture was then stirred at either 40 °C or 60 °C for 2 to 24 h depending on the reaction under investigation. The results are shown below (Table 1). Excellent yields (>99%) were obtained when the reaction was carried out at 60 °C for 20 h or more (entries 2 and 3). As shown, the reactions reach a satisfactory yield after about 4 h (entry 7). An induction period is obviously needed before the reaction reaches a reasonable rate (entry 8). Similar reactions were carried out employing **2**/Pd(OAc)$_2$ as the catalyst precursor. However, a reduction in the efficiency of the catalysis was observed using this L/Pd combination.

Table 1. Amination reactions employing **1**/Pd(OAc)$_2$ or **2**/Pd(OAc)$_2$ as the catalyst at various temperatures and reaction times.

Entry	Time (h)	Temp. (°C)	Yield (%) (L = **1**)[a]	Yield (%) (L = **2**)[b]
1	24	40	67	–
2	24	60	>99	80
3	20	60	>99	–
4	16	60	93	–
5	12	60	94	82
6	8	60	95	–
7	4	60	94	72
8	2	60	52	–

[a] Reaction conditions: 1.0 equiv. of bromobenzene, 1.2 equiv. of morpholine, 1.4 equiv. of base, 1 mL of solvent and 1 mol-% **1**/Pd(OAc)$_2$. Average of two runs. Determined by gas chromatography. [b] 1 mol-% **2**/Pd(OAc)$_2$.

Compound **2** was synthesised according to the procedure shown in the Experimental Section. The identity of **2** was established by spectroscopic means as well as by X-ray diffraction methods. Two distinct chemical shifts at δ = 3.04 and 4.26 ppm were observed for the methylenic protons of **2** by ^{1}H NMR spectroscopy. Large differences in the shifts imply that the back-and-forth motion of the bridging dppm group around the dicobalt fragment is rather slow. The ^{31}P NMR spectrum displays two singlets in a ratio of 2:1 at δ = 39.03 ppm (2 P, dppm) and 42.74 ppm (1P), respectively, for three phosphorus atoms. The ORTEP diagram for **2** is depicted in Figure 1. As revealed from the structure, the pyridyl ring and the phosphanyl group of the bridged alkyne point away from the centre of the molecule to prevent severe steric hindrance. This situation is also true for the coordinated dppm ligand and the P(*t*Bu)$_2$ substituent. All four carbonyls are located at the terminal positions.

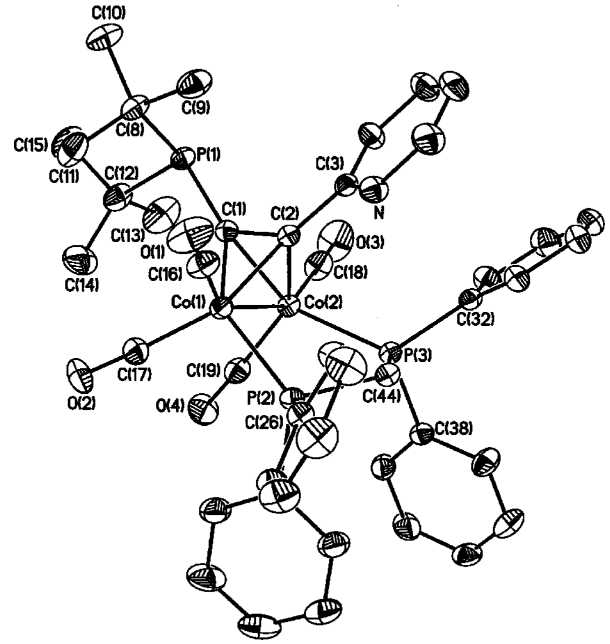


Figure 1. Diagram of **2**. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and bond angles [°]: Co(1)–C(2) 1.946(2); Co(1)–C(1) 2.007(2); Co(1)–P(2) 2.2267(8); Co(1)–Co(2) 2.4876(5); Co(2)–C(2) 1.957(2); Co(2)–C(1) 1.998(3); Co(2)–P(3) 2.2415(8); P(1)–C(1) 1.809(3); P(2)–C(44) 1.828(3); P(3)–C(44) 1.828(3); N–C(3) 1.340(3); C(1)–C(2) 1.359(3); C(2)–C(3) 1.470(4); C(2)–Co(1)–C(1) 40.17(10); C(1)–Co(1)–P(2) 138.98(8); C(1)–Co(1)–Co(2) 51.43(7); C(2)–Co(2)–C(1) 40.17(10); C(1)–Co(2)–P(3) 131.70(8); C(1)–Co(2)–Co(1) 51.76(7); C(2)–C(1)–P(1) 132.4(2); Co(2)–C(1)–Co(1) 76.81(9); C(1)–C(2)–C(3) 136.5(2); Co(1)–C(2)–Co(2) 79.18(9); N–C(3)–C(2) 118.2(2); P(3)–C(44)–P(2) 109.79(15).

For comparison, similar reactions were carried out using Pd(OAc)$_2$ complexes chelated with **3** or **4** as catalyst precursors. In these cases, higher reaction temperatures of 80 °C and longer reaction times of 16 h were required for the reactions to be reasonably efficient. Generally speaking, amination reactions carried out employing **3**- or **4**/Pd(OAc)$_2$ as the catalytic systems are not as effective as those based on **1**/Pd(OAc)$_2$ (Table 2). These experimental observations are consistent with the commonly accepted idea that a phosphane ligand with bulky *t*Bu substituents is generally more efficient than that with a less bulky Cy or *i*Pr group.[8a,10]

Table 2. Reactions employing **3**/Pd(OAc)$_2$ or **4**/Pd(OAc)$_2$ as a catalyst at various reaction temperatures and times.

Entry	Time (h)	Temp. (°C)	Yield (%) (L = **3**)[a]	Yield (%) (L = **4**)[b]
1	4	60	20	–
2	6	60	21	–
3	6	80	52	25
4	8	80	53	31
5	10	80	62	47
6	14	80	74	62
7	16	80	85	82

[a] Reaction conditions: 1.0 equiv. of bromobenzene, 1.2 equiv. of morpholine, 1.4 equiv. of base, 1 mL of solvent and 1 mol-% **3**/Pd(OAc)$_2$. Average of two runs. Determined by gas chromatography. [b] 1 mol-% **4**/Pd(OAc)$_2$.

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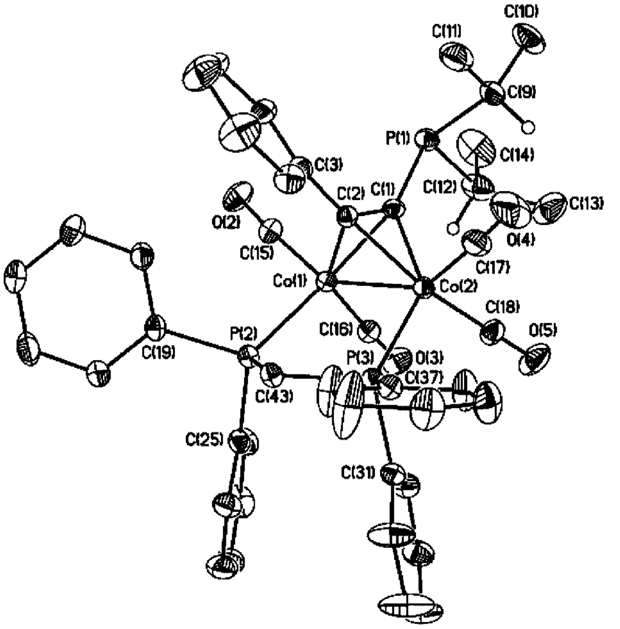

Figure 2. Diagram of **4**. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and bond angles [°]: Co(1)–C(1) 1.959(4), Co(1)–C(2) 1.978(4), Co(1)–P(2) 2.2427(10), Co(1)–Co(2) 2.4896(7), Co(2)–C(2) 1.951(3), Co(2)–C(1) 1.984(3), Co(2)–P(3) 2.2253(10), P(1)–C(1) 1.795(3), P(2)–C(43) 1.841(3), P(3)–C(43) 1.840(4), C(1)–C(2) 1.351(5), C(2)–C(3) 1.478(5), C(1)–Co(1)–C(2) 40.13(14), C(1)–Co(1)–P(2) 139.80(11), C(2)–Co(1)–P(2) 101.18(10), C(1)–Co(1)–Co(2) 51.30(10), C(2)–Co(1)–Co(2) 50.21(10), P(2)–Co(1)–Co(2) 99.21(3), C(2)–Co(2)–C(1) 40.15(14), C(1)–Co(2)–P(3) 138.94(11), C(2)–Co(2)–Co(1) 51.17(10), C(1)–Co(2)–Co(1) 50.41(11), C(43)–P(2)–Co(1) 108.62(12), C(43)–P(3)–Co(2) 110.70(11), C(2)–C(1)–P(1) 137.7(3), C(2)–C(1)–Co(1) 70.7(2), C(2)–C(1)–Co(2) 68.6(2), P(1)–C(1)–Co(2) 142.8(2), Co(1)–C(1)–Co(2) 78.29(12), C(1)–C(2)–C(3) 137.1(3), C(1)–C(2)–Co(2) 71.2(2), C(1)–C(2)–Co(1) 69.2(2), Co(2)–C(2)–Co(1) 78.62(13), O(2)–C(15)–Co(1) 176.0(4), P(2)–C(43)–P(3) 110.73(18).

Compound **4** was prepared and characterised by spectroscopic means. Its crystal structure was also determined by X-ray diffraction methods (see below). In the ^{1}H NMR spectrum of **4**, two distinct chemical shifts at δ = 3.27 and 3.42 ppm were observed for the methylenic protons. In addition, the ^{31}P NMR spectrum displays two singlets in the ratio of 2:1 at δ = 37.89 ppm (2 P, dppm) and 23.48 ppm (1 P) for three phosphorus atoms. The ORTEP diagram for complex **4** is depicted in Figure 2. The structural features observed in **4** were similar to those observed for **2** except that the *i*Pr groups are not as bulky.

Amination reactions were carried out with various ratios of **1**/Pd(OAc)$_2$ or **3**/Pd(OAc)$_2$ under the reaction conditions shown below (Table 3). The optimum yield was achieved when the reaction was conducted with an NaO*t*Bu / toluent solvent system and a L/Pd(OAc)$_2$ ratio of 1:1 (Table 3, entry 3). The positive role played by the phosphane ligand in the reaction can be clearly seen. No conversion was observed without the presence of phosphane (Table 3, entry 6). Again, better efficiency was obtained by employing **1**/Pd(OAc)$_2$.

Table 3. Reactions employing various ratios of Pd(OAc)$_2$/L.

Entry	L/Pd(OAc)$_2$	Yield (%) (L = **1**)[a]	Yield (%) (L = **3**)[b]
1	2:1	36	54
2	1.5:1	73	62
3	1:1	94	85
4	0.5:1	88	71
5	0.1:1	57	23
6	0:1	0	0

[a] Reaction conditions: 1.0 equiv. of bromobenzene, 1.2 equiv. of morpholine, 1.4 equiv. of NaO*t*Bu, 1 mL of toluene and **1**/Pd(OAc)$_2$ at 60 °C for 4 h. Average of two runs. Determined by gas chromatography. [b] **3**/Pd(OAc)$_2$ at 80 °C for 16 h.

As has been established, a well chosen base/solvent system is essential for the success of an efficient palladium-catalysed coupling reaction. As a consequence, amination reactions of bromobenzene by morpholine employing **1**- or **3**/Pd(OAc)$_2$ as the catalyst precursor with various base/solvent systems were carried out at 60 °C for 4 h (Table 4). As shown, the best base/solvent composition is NaO*t*Bu/toluene (entry 1). This may be partially due to the reductive capacity of NaO*t*Bu in toluene.[11]

Amination reactions of bromobenzene by morpholine employing **1** with various Pd sources in a NaO*t*Bu/toluene system were carried out at 60 °C for 4 h (Table 5). As shown, excellent yields were obtained using Pd(OAc)$_2$ or [(η^3-C$_3$H$_5$)PdCl]$_2$ as palladium sources (entries 1 and 6) and this was true using **1** or **3** as the ligand. However, while the [(η^3-C$_3$H$_5$)PdCl]$_2$ system exhibits good catalytic efficiency, the complex is not suitable for use because of its air-sensitivity. Interestingly, no product was detectable when using PdCl$_2$ as the palladium source (entry 2).

Table 4. Reactions employing Pd(OAc)$_2$/L with various bases and solvents.

Entry	Pd/Ligand	Base	L = **1**[a]		L = **3**[b]	
			Solvent	Yield (%)	Solvent	Yield (%)
1	1:1	NaO*t*Bu	toluene	94	toluene	85
2	1:1	NaO*t*Bu	THF	67	–	–
3	1:1	NaO*t*Bu	DME	30	DME	37
4	1:1	NaO*t*Bu	–	–	DMF	23
5	1:1	KO*t*Bu	toluene	3	toluene	24
6	1:1	KOH	toluene	≈ 1	toluene	0
7	1:1	NaOH	toluene	4	toluene	13
8	1:1	Cs$_2$(CO)$_3$	toluene	0	toluene	8
9	1:1	K$_3$PO$_4$	toluene	0	toluene	0

[a] Reaction conditions: 1.0 equiv. of bromobenzene, 1.2 equiv. of morpholine, 1.4 equiv. of base, 1 mL of solvent and 1 mol-% **1**/Pd(OAc)$_2$ at 60 °C for 4 h. Average of two runs. Determined by gas chromatography. [b] 1 mol-% **3**/Pd(OAc)$_2$ at 80 °C for 16 h.

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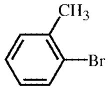
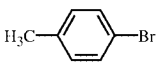
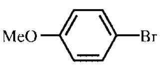
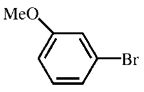
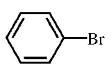
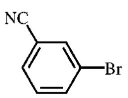
Table 5. Reactions employing various Pd sources.

Entry	Pd source	Yield (%) (L = **1**)[a]	Yield (%) (L = **3**)[b]
1	$Pd(OAc)_2$	94	85
2	$PdCl_2$	0	0
3	$Pd(COD)Cl_2$	19	75
4	$PdCl_2(CH_3CN)_2$	59	68
5	$Pd_2(dba)_3$	2	28
6	$[(\eta^3\text{-}C_3H_5)PdCl]_2$	94	90

[a] Reaction conditions: 1.0 equiv. of bromobenzene, 1.2 equiv. of morpholine, 1.4 equiv. of Na*Ot*Bu, 1 mL toluene and 1 mol-% **1**/$Pd(OAc)_2$ at 60 °C for 4 h. Average of two runs. Determined by gas chromatography. [b] 1 mol-% **3**/$Pd(OAc)_2$ at 80 °C for 16 h.

It has been commonly observed that a better conversion may be reached for an aryl halide with an electron-withdrawing rather than an electron-donating substituent in a palladium-catalysed coupling reaction.[8c] Amination reactions employing **1**/$Pd(OAc)_2$ and aryl bromides, with various electron-withdrawing/donating capacities in a Na*Ot*Bu /toluene system were carried out at 60 °C for 4 h (Table 6). The best yield was obtained for aryl halides with an electron-withdrawing group which is in agreement with the common observation for palladium-catalysed coupling reactions (entry 6). Similar trends were observed when employing **3**/$Pd(OAc)_2$ or **4**/$Pd(OAc)_2$ as the catalyst precursor (Table 6). Interestingly, in our previous work using **4**/$Pd(OAc)_2$ as a catalyst precursor in Suzuki reactions, the catalytic efficiency was rather poor. Nevertheless, the efficiency was comparable with that using **1**- or **2**/$Pd(OAc)_2$ as a precursor in amination reactions.

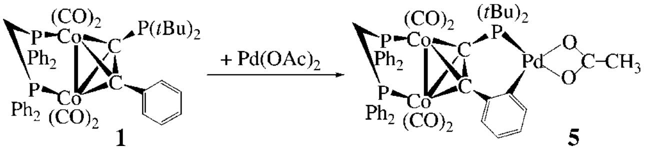
Table 6. Reactions of various aryl bromides employing L/$Pd(OAc)_2$.

Entry	Substrate	Yield (%) (L = 1)[a]	Yield (%) (L = 3)[b]	Yield (%) (L = 4)[c]
1		27	28	17
2		68	66	67
3		95	62	68
4		80	70	42
5		94	85	82
6		99	80	81

[a] Reaction conditions: 1.0 equiv. of bromobenzene, 1.2 equiv. of morpholine, 1.4 equiv. of Na*Ot*Bu, 1 mL of toluene and 1 mol-% **1**/$Pd(OAc)_2$ at 60 °C for 4 h. Average of two runs. Isolated yield. [b] 1 mol-% **3**/$Pd(OAc)_2$ at 80 °C for 16 h. [c] 1 mol-% **4**/$Pd(OAc)_2$ at 80 °C for 16 h.

Characterisation of a Novel Deprotonated Palladium Complex Chelated with 1

Interestingly, a novel palladium complex **5**, namely Pd(OAc) chelated by deprotonated **1**, was obtained from the reaction of **1** with $Pd(OAc)_2$ in toluene at 25 °C for 1 h (Scheme 3). Compound **5** was characterised by spectroscopic means and its crystal structure was determined by X-ray diffraction (Table 7). As revealed by its crystal structure, a process of orthometallation must have occurred which was presumably accompanied by the release of one equiv. of acetic acid (Figure 3). The acetate ligand is coordinated to the palladium through a bidentate chelating mode.[12] The palladium metal centre is in a square planar environment. Two bulky units, $P(tBu)_2$ and dppm, are in *anti* positions. There is one diethyl ether molecule in each asymmetric unit. As has been established, most acetate palladium complexes are dimeric with two acetates bridging two palladium ions. We believe that the formation of this exceptional monomeric structure of **5** is due to the unique bulkiness and bonding mode of ligand **1**. A rather downfield ^{31}P NMR shift at δ = 91.6 ppm was observed which we assigned to the corresponding palladium attached phosphorus site. A triplet signal was observed in the ^{1}H NMR spectrum corresponding to the two methylenic protons of the coordinated dppm. This implies that the coordinated dppm is in a rapid back-and-forth thermal motion. All these spectroscopic data are consistent with the data obtained from the solid-state structure. The crystal structure of **5** also demonstrates that only one molar equivalent of phosphane ligand is needed for effective coordination to a palladium ion. For a conventional PR_3 (R: alkyl or aryl), two or even three ligands are required to sustain a stable palladium complex.



1 **5**

Scheme 3.

Table 7. Amination reactions employing **5** as catalyst.[a]

Entry	**5**/Substrate (mol-%)	Yield (%)
1	0.5	40
2	1	78
3	1.5	>99

[a] Reaction conditions: 1.0 equiv. of aryl halide, 1.2 equiv. of morpholine, 1.4 equiv. of Na*Ot*Bu, 1 mL of toluene at 60 °C for 4 h. Average of two runs. Determined by gas chromatography.

Buchwald has proposed a phosphane ligand coordinated palladium complex **6** as an active species in one of the palladium-catalysed amination reactions.[13] However, nothing further was stated about the bonding mode of the acetate ligand in **6** probably because its crystal structure was not established. By comparing **5** and **6**, the structural similarities for these two compounds are clear (Scheme 4). The

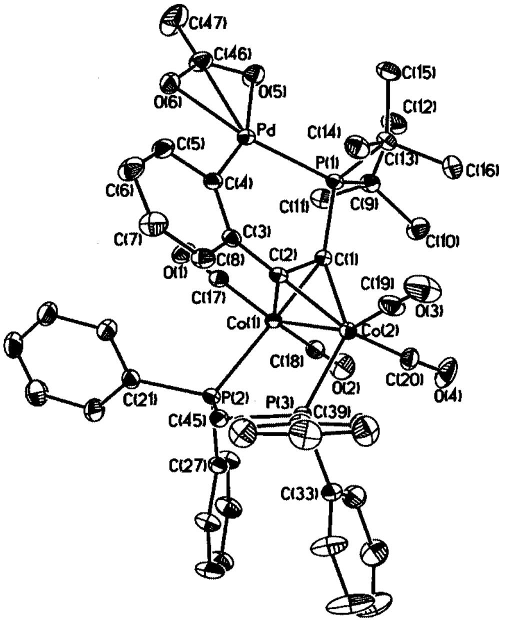
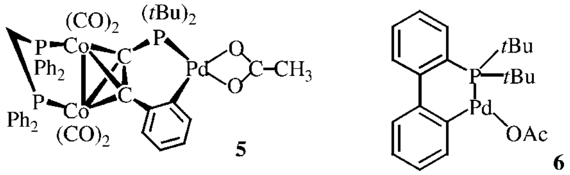


Figure 3. Diagram of **5**. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: Pd–C(4) 2.001(4), Pd–O(5) 2.163(3), Pd–O(6) 2.171(3), Pd–P(1) 2.2182(11), Pd–C(46) 2.509(5), Co(2)–C(1) 1.970(4), Co(2)–P(3) 2.2241(11), Co(2)–Co(1) 2.4764(8), Co(1)–C(2) 1.969(4), Co(1)–C(1) 1.968(4), P(1)–C(1) 1.778(3), O(6)–C(46) 1.240(6), O(5)–C(46) 1.266(7), C(46)–C(47) 1.495(8), C(3)–C(4) 1.405(6), C(3)–C(2) 1.460(5), C(5)–C(4) 1.396(6), C(1)–C(2) 1.362(5), C(4)–Pd–O(5) 161.12(15), C(4)–Pd–O(6) 101.56(15), O(5)–Pd–O(6) 59.92(14), C(4)–Pd–P(1) 92.04(12), O(5)–Pd–P(1) 106.48(11), O(6)–Pd–P(1) 166.39(10), C(2)–Co(2)–C(1) 40.76(15), C(2)–Co(1)–C(1) 40.48(15), C(1)–P(1)–Pd 108.10(13), C(46)–O(6)–Pd 90.5(3), C(46)–O(5)–Pd 90.2(3), O(5)–C(46)–O(6) 119.4(4), C(47)–C(46)–Pd 177.4(6), C(4)–C(3)–C(2) 119.5(3), C(2)–C(1)–P(1) 121.8(3), C(1)–C(2)–C(3) 130.6(3), C(5)–C(4)–C(3) 117.8(4), C(5)–C(4)–Pd 111.1(3), C(3)–C(4)–Pd 131.1(3).

newly characterised compound **5** can be regarded as a more complicated, metal-containing version of **6**.

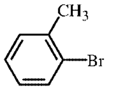
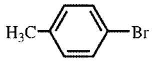
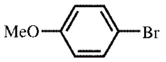
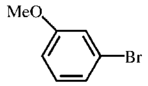
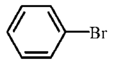
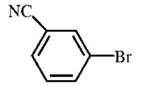


Scheme 4.

Complex **5** was employed as the Pd source for the aminations of bromobenzene by morpholine. Reactions were carried out in an NaO*t*Bu/toluene phase at 60 °C for 4 h (Table 7). The catalytic efficiency of the reaction employing complex **5** is clearly not as good as that carried out in situ (Table 1, entry 7 vs. Table 7, entry 2). It indicates that complex **5** is not a genuinely catalytically active species. Rather, complex **5** could be regarded as the precursor to a genuine catalytically active Pd^0 species. It still requires a reduction process to convert the Pd^{II} to the more active Pd^0 species.[14] Furthermore, the catalytic efficiency could be greatly improved by increasing the molar ratio of **5** (Table 7, entry 3).

For comparison, amination reactions of aryl bromides bearing various electron-withdrawing/electron-donating substituents, with morpholine, employing **5** in a NaO*t*Bu/toluene system, were carried out at 60 °C for 4 h (Table 8). Generally speaking, the efficiencies are lower for **5** than for **1**/Pd(OAc)$_2$ (Table 6 vs. Table 8). The best yield was found in the case of the aryl bromide with an electron-withdrawing group (entry 6).

Table 8. Reactions of various aryl bromides employing **5**.[a]

Entry	Substrate	Yield (%)
1		23
2		64
3		77
4		78
5		80
6		94

[a] Reaction conditions: 1.0 equiv. of aryl halide, 1.2 equiv. of morpholine, 1.4 equiv. of base and 1 mL of solvent. Average of two runs. Isolated yield.

Concluding Remarks

We have demonstrated that the amination reactions of aryl bromides by morpholine can be carried out catalytically with palladium complexes modified with a novel cobalt-containing phosphane ligand **1**. The catalytic performance is best with a **1**/Pd(OAc)$_2$ ratio of 1:1. The same reactions may also be carried out using palladium complexes modified with **2**, **3** or **4** but with reduced efficiency.

A novel palladium complex **5** was obtained from the reaction of **1** with Pd(OAc)$_2$. As revealed by the crystal structure, a process of orthometallation occurs presumably accompanied by the release of one equiv. of acetic acid. We propose that **5** could be the precursor to the true catalytically active Pd^0 species.

Experimental Section

Synthesis of (μ-PPh$_2$CH$_2$PPh$_2$)Co$_2$(CO)$_4$[μ,η-PyC≡CP(*t*Bu)$_2$] (2): Dicobalt octacarbonyl Co$_2$(CO)$_8$ (1.00 mmol, 0.34 g), dppm (1.00 mmol, 0.38 g) and toluene (10 mL) were placed in a 100 mL capacity round flask charged with a magnetic stirrer. The solution was stirred at 65 °C for 6 h and a yellow coloured compound, Co$_2$(CO)$_6$(μ-P,P-dppm), was produced. Without further separation, the reaction flask was then charged with one equiv. of

PyC≡CP(tBu)$_2$ (0.25 g) in toluene (5 mL). Subsequently, the solution was stirred at 80 °C for 16 h before the solvent was removed under reduced pressure. The residue was further separated by CTLC. A dark green coloured band was eluted using a mixed solvent mobile phase (CH$_2$Cl$_2$/hexane, 1:3) and was identified as **2**. The yield was 72% (0.62 g, 0.72 mmol). ^{1}H NMR (CDCl$_3$): δ = 6.90–8.50 (m, 24 H, arene), 3.04 (q, 1 H, dppm), 4.26 (q, 1 H, dppm), 1.23 ppm [d, 18 H, P(tBu)$_2$]. ^{31}P NMR (CDCl$_3$): δ = 39.03 (s, 2 P, dppm), 42.74 ppm [s, 1 P, P(tBu)$_2$]. ^{13}C NMR (CDCl$_3$): δ = 127.86–133.07 (29 C, arene), 30.43 ppm (1 C, dppm). $C_{44}H_{44}Co_2NO_4P_3$: calcd. C 60.91, H 5.11; found C 61.34, H 5.15. MS (EI): m/z = 862 [M]$^+$

Synthesis of (μ-PPh$_2$CH$_2$PPh$_2$)Co$_2$(CO)$_4$[μ,η-PyC≡CP(iPr)$_2$] 4: Dicobalt octacarbonyl, Co$_2$(CO)$_8$ (1.00 mmol, 0.34 g), dppm (1.00 mmol, 0.39 g) and toluene (10 mL) were placed in a 100 mL capacity round flask containing a magnetic stirrer. The solution was stirred at 65 °C for 6 h during which time a yellow coloured compound, Co$_2$(CO)$_6$(μ-P,P-dppm), was formed. Without further separation, the reaction flask was charged with one equiv. of PyC≡CP(iPr)$_2$ (0.22 g) in toluene (5 mL) and the solution was then stirred at 80 °C for 16 h. The solvent was removed under reduced pressure and the resultant dark red coloured residue was separated by CTLC. A dark red band was eluted out using mixed solvent mobile phase (CH$_2$Cl$_2$: hexane = 1:3) and the compound was identified as **4**. The yield was 82.0% (0.69 g, 0.82 mmol). ^{1}H NMR (CDCl$_3$): δ = 7.77–7.00 (m, 25 H, arene), 3.27–3.42 (d, 2 H, CH$_2$), 2.23–2.25 (m, 2 H), 1.23–1.43 ppm [m,12 H, P(iPr)$_2$]. ^{31}P NMR (CDCl$_3$): δ = 37.89 (s, 2 P, dppm), 23.48 ppm [s, 1 P, P(iPr)$_2$]. $C_{43}H_{41}Co_2O_4P_3$: calcd. C 61.95, H 4.90; found: C 62.03, H 4.96.

Synthesis of [(μ-PPh$_2$CH$_2$PPh$_2$)Co$_2$(CO)$_4${μ,η-PhC≡CP(tBu)$_2$}]-PdOAc (5): The two reactants, Pd(OAc)$_2$ (1.00 mmol, 0.22 g) and [(μ-PPh$_2$CH$_2$PPh$_2$)Co$_2$(CO)$_4${μ,η-PhC≡CP(tBu)$_2$}] **1** (1.00 mmol, 0.86 g) were placed in a 100-mL round-bottomed flask charged with a magnetic stirrer and toluene (5 mL). The solution was stirred at 25 °C for 1 h before the solvent was removed in vacuo. The crude material was further purified by CTLC. A red-brown band was eluted with CH$_2$Cl$_2$ and was identified as **5**. The yield was 80% (0.82 g, 0.80 mmol). ^{1}H NMR (CDCl$_3$): δ = 7.54–6.92 (24 H, arene), 3.30 (t, J_{PH} = 10.2 Hz, 2 H, CH$_2$), 1.53 ppm (d, J_{PH} = 7 Hz, 18 H, tBu). ^{13}C NMR (CDCl$_3$): δ = 137.16–124.92 (30 C, arene), 41.32 (t, 1 C, CH$_2$), 38.93 [d, 2 C, -C(CH$_3$)$_3$], 30.55 [d, 6 C, -C(CH$_3$)$_3$], 67.97 ppm [s, 1 C, PhC≡CP(tBu)$_2$]. ^{31}P NMR (CDCl$_3$): δ = 38.8 (s, 2 P, dppm), 91.6 ppm [s, 1 P, P(tBu)$_2$]. MS (ESI): m/z = 1024 [M]$^+$. $C_{51}H_{57}Co_2O_7P_3Pd$: calcd. C 55.07, H 4.62; found: C 53.85, H 4.63.

Amination of Aryl Bromides

Method: An oven-dried Schlenk tube was charged with **1** (8.60 mg, 0.01 mmol), Pd(OAc)$_2$ (2.24 mg, 0.01 mmol) and base (1.4 mmol). The tube was evacuated, filled with nitrogen and then the aryl bromide (1.00 mmol), toluene (1 mL) and morpholine (1.20 mmol) were added. The tube was sealed with a Teflon screw cap and the mixture was stirred at 60 °C for 4 h. After all the starting materials had been consumed, the mixture was cooled to room temperature and was then diluted with diethyl ether (40 mL). The resultant suspension was transferred to a separating funnel and washed with water (10 mL). The organic layer was separated, dried with anhydrous MgSO$_4$ and concentrated in vacuo. The crude residue was purified by CTLC with a mixture of hexane/ethyl acetate as the mobile phase.

The couplings of morpholine with bromobenzene, 4-bromotoluene, 3-bromoanisole or 3-chloronitrobenzene were examined using the method. The isolated yields of the corresponding products, *N*-phenylmorpholine, *N*-(4-methyl)phenylmorpholine, *N*-(3-methoxyphenyl)morpholine and *N*-(3-nitrophenyl)morpholine were 94% (0.153 g), 68% (0.120 g), 80% (0.155 g) and 99% (0.206 g), respectively.

***N*-Phenylmorpholine:** ^{1}H NMR (CDCl$_3$): δ = 6.88–6.93, 7.25–7.30 (m, 5 H), 3.87 (t, 4 H, J = 2.4 Hz), 3.16 ppm (t, 4 H, J = 2.6 Hz).

***N*-(4-Methylphenyl)morpholine:** ^{1}H NMR (CDCl$_3$): δ = 3.10 (t, 4 H, J = 5 Hz), 3.86 (t, 4 H, J = 4.6 Hz), 6.83 (d, 2 H, J = 8.6 Hz), 7.10 ppm (d, 2 H, J = 8.4 Hz).

Table 9. Crystal data for **2**, **4** and **5**.

Compound	**2**	**4**	**5**
Formula	$C_{44}H_{44}Co_2NO_4P_3$	$C_{43}H_{41}Co_2O_4P_3$	$C_{51}H_{57}Co_2O_7P_3Pd$
Formula weight	861.57	832.53	1099.14
Crystal system	monoclinic	monoclinic	monoclinic
Space group	$P2_1/c$	$P2_1/c$	$P2_1/c$
a (Å)	13.8627(12)	16.0552(12)	13.6654(17)
b (Å)	14.1883(12)	11.6582(9)	17.291(2)
c (Å)	21.8278(19)	23.1912(18)	22.379(3)
α (°)	90	90	90
β (°)	96.748(2)	109.574(2)	102.903(2)
γ (°)	90	90	90
V (Å^3)	4263.5(6)	4089.9(5)	4858.2(14)
Z	4	4	4
D_c (Mg m^{-3})	1.342	1.352	1.416
λ (Mo-K_α) [Å]	0.71073	0.71073	0.71073
μ (mm^{-1})	0.932	0.968	1.122
θ range [°]	2.06 to 26.01	1.86 to 26.02	1.87 to 26.11
Observed reflections [$F > 4\sigma(F)$]	8354	8001	10219
No. of refined parameters	495	469	577
R_1 for significant reflections[a]	0.0373	0.0469	0.0429
wR_2 for significant reflections[b]	0.0852	0.1649	0.1494
GoF[c]	0.947	1.618	1.035

[a] $R_1 = |\Sigma(|F_o| - |F_c|)/|\Sigma F_o||$. [b] $wR_2 = \{\Sigma[w(F_o^2 - F_c^2)]^2/\Sigma[w(F_o^2)^2]\}^{1/2}$; w = 0.0497, 0.0731 and 0.1277 for **2**, **4** and **5**, respectively. [c] GoF = $[\Sigma w(F_o^2 - F_c^2)^2/(\text{number of reflections} - \text{number of parameters})]^{1/2}$.

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***N*-(3-Methoxyphenyl)morpholine:** ^{1}H NMR ($CDCl_3$): δ = 3.15 (t, 4 H, J = 2.4 Hz), 3.85 (t, 4 H, J = 2.4 Hz), 6.45 (d, 1 H, J = 3.6 Hz), 6.54 (d, 1 H, J = 4.0 Hz), 7.20 ppm (t, 2 H, J = 4.0 Hz).

***N*-(3-Nitrophenyl)morpholine:** ^{1}H NMR ($CDCl_3$): δ = 3.18 (t, 4 H, J = 2.4 Hz), 3.87 (t, 4 H, J = 2.4 Hz), 7.10–7.14 (m, 3 H), 7.34 ppm (t, 1 H, J = 3.8 Hz).

4-Methoxyphenylmorpholine: ^{1}H NMR ($CDCl_3$): δ = 6.84–6.91 (m, 4 H), 3.76 (s, 3 H), 3.78–3.87 (m, 4 H), 3.05–3.07 ppm (m, 4 H).

X-ray Crystallographic Studies: Suitable crystals of **2**, **4** and **5** were sealed in thin-walled glass capillaries under nitrogen and mounted on a Bruker AXS SMART 1000 diffractometer. Intensity data were collected from 1350 frames with increasing ω (width of 0.3° per frame). The absorption correction was based on the symmetry equivalent reflections using the SADABS program. The space group determination was based on a check of the Laue symmetry and systematic absences and was confirmed using the structure solution. The structure was solved by direct methods using the SHELXTL package.[15] All non-hydrogen atoms were located from successive Fourier maps and the hydrogen atoms were refined using a riding model. Anisotropic thermal parameters were used for all non-hydrogen atoms and fixed isotropic parameters were used for H atoms.[16] The crystallographic data of **2**, **4** and **5** are summarised in Table 9.

Crystallographic data for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre. CCDC-261777, -261778 and -261779 for compounds **2**, **4** and **5**, respectively, 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.

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[16] The hydrogen atoms were allowed to ride on carbon atoms or oxygen atoms in their idealised positions and were held fixed with C–H distances of 0.96 Å.

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