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PAPER

Palladium(II) thiocarboxamide complexes: synthesis, characterisation and application to catalytic Suzuki coupling reactions†

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A simple route to synthesise palladium(II) complexes from the reaction of N-substituted pyridine-2-thiocarboxamide ligands and $PdCl_2(PPh_3)_2$ has been developed. The new complexes are very soluble in common solvents and have been fully characterised (elemental analysis, FT-IR, ^1H, ^{31}P, ^{13}C-NMR), including an X-ray diffraction analysis. The molecular structures of all the complexes were determined and reveal the presence of square planar geometry around Pd with little distortion. The complexes were tested in the Suzuki coupling of electronically deactivated aryl and heteroaryl bromides and were found to have much greater activity, without using any promoting additives or phase transfer agent under aerobic conditions. Higher reaction rates are obtained by varying R substituents on the aromatic ring of pyridine-2-thiocarboxamide. The effect of other variables on the cross-coupling reaction, such as temperature, solvent and base, is also reported.

Introduction

The synthesis of biaryls has been commonly applied in a variety of contexts, ranging from natural-products synthesis to materials chemistry (polymers, dendrimers and nanostructured materials) as well as in fine chemistry (agrochemicals, pharmaceuticals), including large-scale production.[1] In this regard, the procedures familiarised by Suzuki,[2] Stille,[3] Ullmann,[4] Negishi,[5] Semmelhack,[6] Kharasch,[7] Meyers,[8] and Lipshutz[9] have become modern tools in the chemist's repertory. Among the fascinating attributes of the Suzuki reaction are a wide availability due to low toxicity of boronic acids, stability to the atmosphere, and the facile removal of the boron-containing side products (Scheme 1). The exemplary approach of performing this reaction is to employ aryl halides and organometals containing magnesium, zinc or boron in the presence of palladium catalysts. It is known that various palladium[10] and nickel-based[11] catalysts and nanosized palladium[12] are also very effective with aryl halides. Recently significant process has been made toward activation of aryl halides through the use of various alkylphosphine ligands in the coupling reaction.[13] However, lately, the most developed and studied catalysts for the formation of biaryls are palladacycles.[14]

Palladium(II) thiosemicarbazone complexes are active catalysts in carbon–carbon coupling reactions such as the Suzuki reaction and the Heck reaction.[15] Babak Karimi and co-workers have reported an efficient and recyclable water-soluble NHC–Pd polymer catalyst for the Suzuki coupling of aryl chlorides in water at room temperature.[16] Hyunmin Yi and co-workers have reported a Suzuki coupling reaction of aryl iodides with arylboronic acids using viral-templated palladium nanocatalysts.[17] The use of a palladium–guanidine complex immobilised on SBA-16 as a highly active and recyclable catalyst for Suzuki coupling for various aryl bromides and arylboronic acids under mild conditions has been described.[18] Palladium(0) complex catalysed regiocontrolled Sonogashira and Suzuki cross-coupling reactions *via* a one-pot double-coupling approach have been reported.[19] In addition, a phosphine-free carbonylative cross-coupling reaction of aryl iodides with arylboronic acids catalysed by immobilisation of palladium in MCM-41 has been studied.[20] A palladium N-heterocyclic carbene complex was used as an efficient catalyst for the activation of aryl chlorides at room temperature.[21] A solid slide coated with a multilayered palladium–pyridyl complex has been used as an efficient catalyst for various aryl halides and arylboronic acids for Suzuki coupling.[22] Further, Suzuki coupling reactions of aryl halides with

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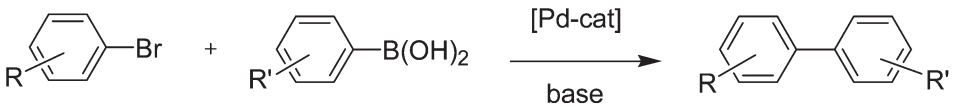
†Electronic supplementary information (ESI) available: ^1H, ^{31}P, ^{13}C-NMR data and spectra, IR and Elemental analysis data. CCDC 852894, 852895, 830763 and 830766. For ESI and crystallographic data in CIF or other electronic format see 10.1039/c2dt12243j



Scheme 1 The Suzuki biaryl coupling reaction.

arylboronic acids were successfully carried out with monodispersed Pd nanoparticles on diamine functionalised LDH.[23] Furthermore, Vivek Polshettiwar, Aziz Fihri and co-workers reported Suzuki–Miyaura cross-coupling reactions of deactivated aryl chloride in water with low catalyst loading, without using any phase transfer reagent.[24] Among different ligand systems of palladium the most efficient catalytic systems are palladium–phosphine complexes and palladacycles.

Nowadays, the most important challenge is the development of a ubiquitous method for the cross-coupling of nitrogen containing heterocycles.[25] Nitrogen-based heterocycles are pervasive in biologically active compounds, but particularly detrimental to catalyst activity when palladium is used.[26] The presence of such groups, which are particularly widespread in medicinal chemistry,[27] can lead to less reactivity in coupling reactions. In addition, the Suzuki reaction is an efficient method in the area of drug developments including nitrogen heterocycles as substrates.

In N-substituted pyridine-2-thiocarboxamide ligands, a variety of amines are used to tune the steric and electronic properties of the products. Such ligands have the potential to coordinate to metal centres in different ways, such as deprotonation of the ligand, which may occur prior to coordination, and because thioamides have two tautomeric forms they may act as either a monoanionic *N*,*N* (coordination of thioketo tautomer) or *S*,*N* (coordination of the thiol form) bidentate ligand. Alternatively, the neutral ligand may coordinate to the metal centre *via* the pyridyl nitrogen and sulfur atoms. However, coordination *via* the amide nitrogen and the sulfur (either as the neutral ligand or after deprotonation) would give four-membered metallacycles. In the case of the deprotonated ligand both tautomeric forms will again be possible but in the case of the protonated ligand only the thioketo isomer is formed (Scheme 2). Palladium(II) complexes have been reported as pincer ligands for the three coordination modes,[28] and gold(III) has been reported for the bidentate coordination.[29] Further, a number of Pd(II) complexes bearing bidentate thiocarboxamides have been synthesised and characterised.[30] Platinum(II) complexes also exist with the ligand, coordinated *via* either the *S*,*N* or *N*,*N* binding modes.[31]

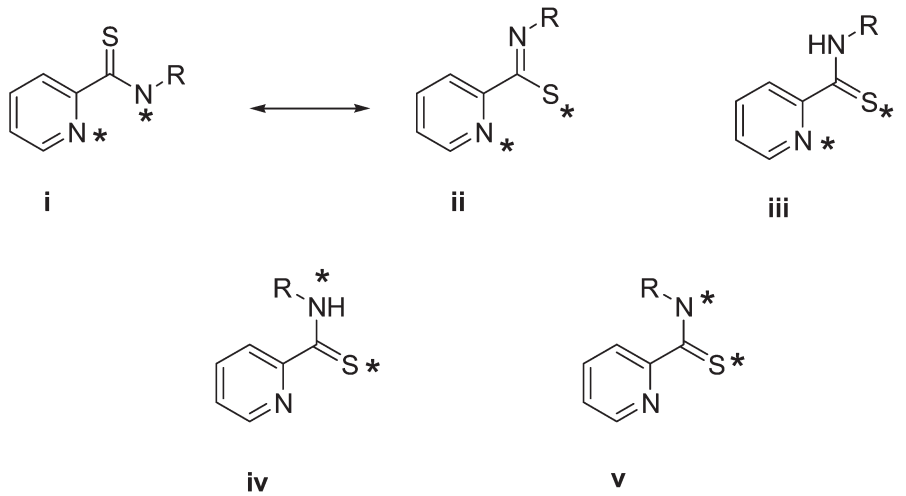
To the best of our knowledge, the use of palladium(II) complexes containing thiocarboxamides as catalysts in Suzuki coupling have not been investigated. In this paper, we report the synthesis and characterisation of new palladium(II) thiocarboxamide complexes. The most interesting features of these catalysts are: (i) the relative insensitivity to the presence of deactivating groups on the aryl and heteroaryl bromide, (ii) the good stability under an atmosphere of air and (iii) the good conversion attainable with a wide variety of substrates upon a suitable choice of the reaction conditions. The evaluation of catalysts and optimisation of the reaction for the coupling of aryl and heteroaryl bromides with arylboronic acids have been carried out.

Results and discussion

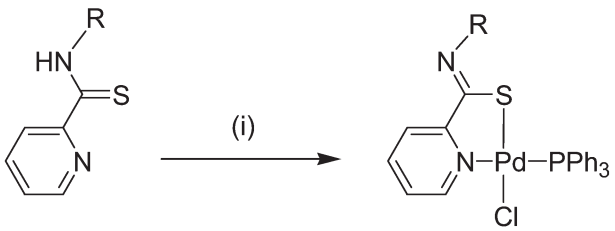
Synthesis and characterisation of the complexes

The N-substituted pyridine-2-thiocarboxamide ligands **1a–d** were prepared as reported in the literature,[32] by reaction of the appropriate aniline with 2-methyl pyridine in the presence of $Na_2S{\cdot}9H_2O$ and sulphur at reflux temperature. The new palladium catalyst precursors of the type [Pd(Cl)(PPh_3)(L)] were synthesised by reacting pyridine-2-thiocarboxamide ligands **1a–d** with one equivalent of $PdCl_2(PPh_3)_2$ in ethanol under reflux for 3 h (Scheme 3).

Coordination by sulfur and nitrogen induces changes in the position and intensity of the bands and the proximity of the phenyl ring bands (triphenylphosphine ligand) makes it difficult to clearly assign the vibration modes in IR spectra. The disappearance of the C=S band observed in the free ligand correlates with the loss of double-bond character upon deprotonation of the N–H group. This supports the lengthening of the C–S bond which we observe in representative molecular structures. For thiocarboxamides bonding in the thiolate form, the C=S band generally shifts to lower energy in the region 820–790 cm^{-1}. These observations may be attributed to the enolisation of –NH–C=S and subsequent coordination through the deprotonated sulphur.[33] The IR spectra of the complexes did not display ν(S–H) at 2585–2570 cm^{-1} suggesting the deprotonation of the thiol proton prior to coordination. Moreover, a new band is appeared around 1281–1267 cm^{-1} which corresponds to ν(C–S) for the thiocarboxamide complexes. In addition, other characteristic



Scheme 2 Possible coordination modes of N-substituted pyridine-2-thiocarboxamide ligands.



1 2

a: R = 2-Cl-Ph, **b:** R = 2-Me-Ph, **c:** R = 4-Me-Ph, **d:** R = 4-Py

Scheme 3 The formation of palladium catalyst precursors of the type [Pd(Cl)(PPh_3)(L)]. Conditions: (i) [$PdCl_2(PPh_3)_2$], ethanol, 80 °C, 3 h.

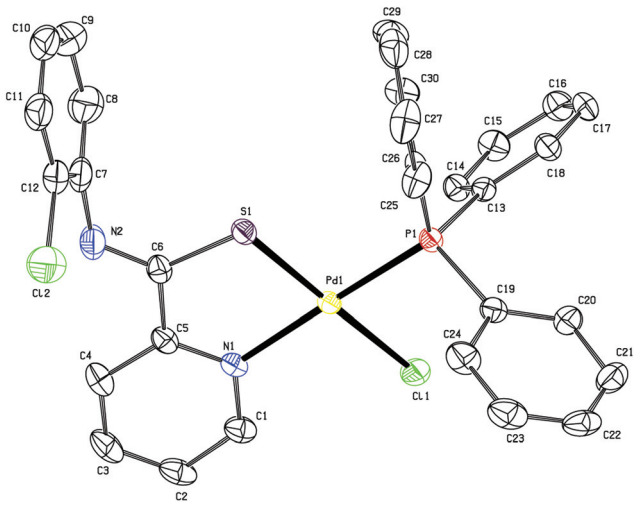


Fig. 1 The molecular structure of [Pd(Cl)(PPh_3)(L1)], **2a**.

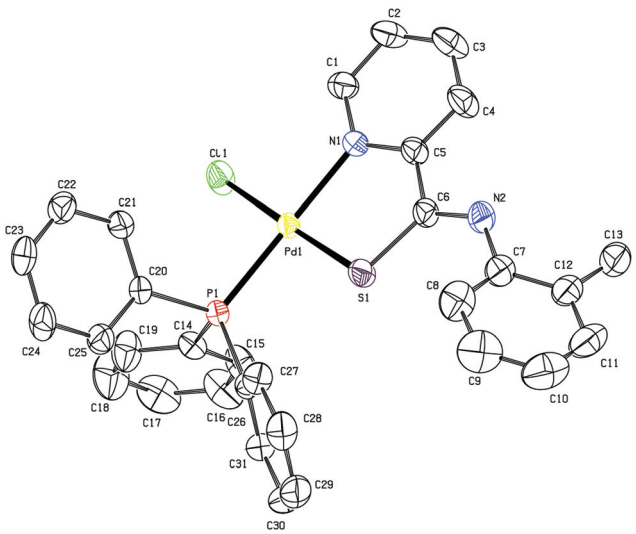


Fig. 2 The molecular structure of [Pd(Cl)(PPh_3)(L2)], **2b**.

bands due to triphenylphosphine are also present around 1436 cm^{-1} in the spectra of all the complexes.[34] A weak intensity band is observed at 1093 cm^{-1} characteristic of the coordinated pyridine.[35] The ^{31}P NMR spectra for all the complexes **2a–d**, show a singlet in the range δ 30.59–31.03 ppm indicating the presence of one PPh_3 group in the complexes. The ^{1}H NMR spectra of the complexes reveal that the coordination of the palladium atom to the pyridyl nitrogen causes a significant downfield shift for the proton adjacent to the nitrogen (H-1), in the range δ 9.58–9.79 ppm. The amide proton is lost upon coordination and is not observed in the spectra of the palladium(II) complexes. All the complexes show a multiplet in the range δ 6.85–8.34 ppm for the aromatic protons including triphenylphosphine and a singlet around δ 2.10 ppm and δ 2.25 ppm in the complexes **2b** and **2c**, respectively, for the methyl protons. In ^{13}C NMR spectra the signal assigned to the thioketone carbon, which moves upfield from δ 190–180 ppm in the ligand to δ 149–161 ppm in the palladium(II) complexes, results from the reduced C–S bond order on coordination.

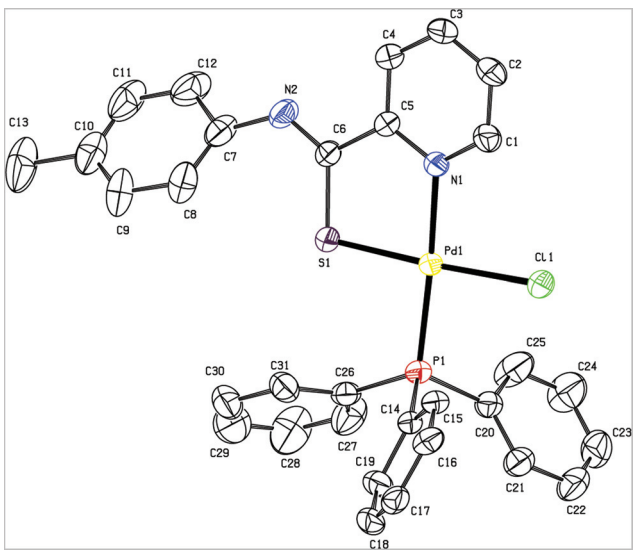


Fig. 3 The molecular structure of [Pd(Cl)(PPh_3)(L3)], **2c**.

X-ray molecular structures

The molecular structures of all the complex **2a–d** were determined and are shown in Fig. 1–4, and selected bond angles and bond distances are gathered in Table 1. The complex **2a** crystallises in the '*pbca*' space group. The palladium centre adopts approximately a square planar coordination geometry, which

confirms that the ligands are coordinated to palladium as their deprotonated thiol tautomer, through the sulfur and the pyridyl nitrogen atom and the remaining two coordination sites are occupied by chloride and triphenylphosphine ligands. The thiocarboxamide ligand binds the metal center at N and S forming one five membered chelate ring with bite angles of 85.17(7)° N(1)–Pd(1)–S(1), 94.54(3)° S(1)–Pd(1)–P(1), 94.10(7)° N(1)–Pd(1)–Cl(1) and 86.36(3)° P(1)–Pd(1)–Cl(1). The bond lengths of Pd(1)–N(1) and Pd(1)–S(1) are 2.104(3) and 2.2633(8) Å, respectively. These bond distances are very similar to those observed in other palladium(II) complexes.[36] Further, the Pd(1)–P(1) bond length of 2.2494(8) Å is in agreement with other structurally characterised palladium–phosphine complexes.[37] Further, it was observed that the complexes **2b–d**, adopt a similar geometry as in the complex **2a**, with slight changes in bond angles and bond distances.

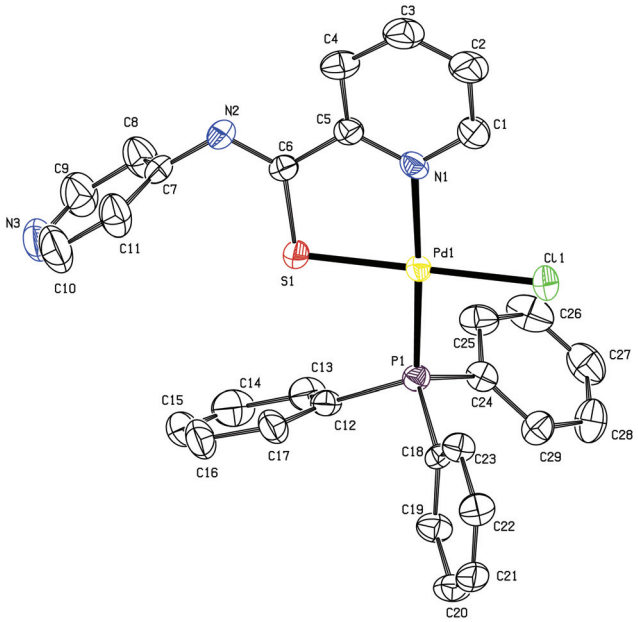


Fig. 4 The molecular structure of [Pd(Cl)(PPh_3)(L4)], **2d**.

Catalytic studies

Inspection of the literature reveals that there is not a set rule that a specific solvent and a certain base are used to attain the highest efficiency of catalysts in Suzuki coupling reactions. We have performed the Suzuki coupling of aryl and heteroaryl bromides with arylboronic acids using all Pd(II) thiocarboxamide complexes as catalysts. In order to optimise the reaction conditions, we initially carried out the reaction of *p*-bromoanisole with phenylboronic acid using complex **2a** (0.1 mol%) as a test catalyst. First the reaction was conducted without any base and no reaction (NR) was observed. Then several bases were tested and a

Table 1 Selected bond lengths (Å) and angles (°) for the complexes **2a–d**

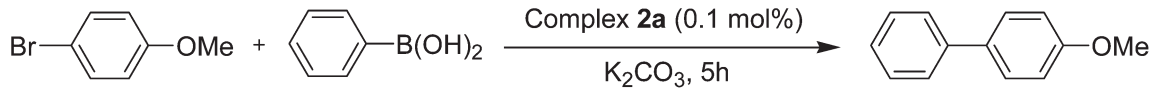
Complex	**2a**	**2b**	**2c**	**2d**
Pd(1)–N(1)	2.104(3)	2.1102(16)	2.105(2)	2.100(5)
Pd(1)–S(1)	2.2633(8)	2.2486(6)	2.2557(8)	2.2491(15)
Pd(1)–P(1)	2.2494(8)	2.2624(5)	2.2608(8)	2.2368(17)
Pd(1)–Cl(1)	2.3374(8)	2.3403(6)	2.3379(9)	2.3304(15)
S(1)–C(6)	1.759(3)	1.756(2)	1.754(3)	1.739(6)
N(2)–C(6)	1.277(4)	1.277(3)	1.269(4)	1.288(7)
N(1)–Pd(1)–S(1)	85.17(7)	84.75(5)	84.66(7)	84.88(13)
N(1)–Pd(1)–P(1)	177.23(7)	175.24(5)	176.51(7)	176.75(13)
S(1)–Pd(1)–P(1)	94.54(3)	92.09(2)	92.73(3)	91.87(6)
N(1)–Pd(1)–Cl(1)	94.10(7)	93.60(5)	93.20(7)	95.52(13)
S(1)–Pd(1)–Cl(1)	176.52(3)	174.15(3)	175.45(4)	179.07(8)
P(1)–Pd(1)–Cl(1)	86.36(3)	89.89(2)	89.56(3)	87.73(6)
C(5)–N(1)–Pd(1)	118.6(2)	118.36(14)	118.8(2)	119.2(4)
C(6)–S(1)–Pd(1)	99.61(11)	101.15(8)	100.63(11)	100.74(19)

Table 2 The effect of the base on Suzuki coupling[a]

Entry	Base	Yield (%)[b]
1	NaOH	60
2	KOH	57
3	Na_2CO_3	68
4	K_2CO_3	69
5	K_3PO_4	66
6	CH_3COONa	36

[a] Conditions: 4-bromoanisole (2.0 mmol), phenylboronic acid (3.0 mmol), 0.1 mol% **2a**, 150 °C, 5 h. [b] Isolated yields.

Table 3 Effect of the solvent on Suzuki coupling[a]



Entry	Solvent	Yield (%)[b]
1	Toluene	85
2	*p*-Xylene	80
3	THF	10
4	Dioxane	42
5	DMAc	36
6	DMSO	13
7	DMF	69
8	NMP	72
9	Dioxane–H_2O (95 : 5)	76

[a] Conditions: 4-bromoanisole (2.0 mmol), phenylboronic acid (3.0 mmol), 0.1 mol% **2a**, K_2CO_3 (4.0 mmol), reflux, 5 h. [b] Isolated yields.

Table 4 The effect of the temperature and time on Suzuki coupling[a]

Entry	Temp (°C)	Time (h)	Yield (%)[b]
1	20	3	11
2	20	5	26
3	40	5	57
4	60	5	68
5	80	3	74
6	80	5	85

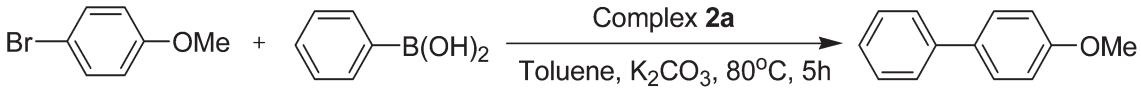
[a] Conditions: 4-bromoanisole (2.0 mmol), phenylboronic acid (3.0 mmol), 0.1 mol% **2a**, K_2CO_3 (4.0 mmol), toluene (20 ml). [b] Isolated yields.

good to excellent yield of the coupling products was observed in all cases (Table 2). The optimisation of bases, which was studied with DMF as solvent, showed K_2CO_3, Na_2CO_3, and K_3PO_4 as the inorganic bases to choose, although biphenyl was obtained as a byproduct in some of the cases. Other bases such as NaOH, KOH and weak inorganic base such as NaOAc were substantially less effective, and weak organic bases such as TEA, piperidine and pyrrolidine failed to promote the reaction, probably because of their ability to bind strongly to palladium. The use of inorganic bases such as carbonates or phosphates allows us to obtain much higher reaction rates, since the best activity is achieved employing the lesser basic carbonates. It is worth noting here that the best reaction rates are obtained using the inexpensive sodium or potassium carbonates.

The solvent effect on the reaction rate of coupling has been studied using a various solvents (Table 3). We investigated apolar solvents such as toluene and *p*-xylene (entries 1 and 2) with K_2CO_3 as base and in the presence of complex **2a** (0.1 mol %), both solvents gave high conversions of *p*-methoxybiphenyl accompanied by considerable amounts of biphenyl. Next, we examined different highly polar solvents and the catalytic activity of the complex is found to be lower, possibly owing to the coordinating properties of these solvents. Reactions conducted were not efficient in THF and DMSO and poor yields obtained when dioxane and DMAc were the solvents of choice (entries 4 and 5). The reaction was more efficient in DMF (69%) or NMP (72%) but still with significant amounts of biphenyl as a byproduct (entries 7 and 8). The dioxane–H_2O solvent system with K_2CO_3, however, gave fairly good product yields.

The occurrence of catalyst deactivation is further supported by the issues of the studies of the temperature influence on the catalysis. Catalyst deactivation has been previously noticed in Suzuki coupling by several authors and, in particular, Bedford has pointed out the importance of the catalyst longevity in order to achieve high substrate conversions and product yields.[38,39] The use of mild reaction conditions is essential with substrates bearing thermally unstable functional groups, and therefore the development of systems active at low temperatures is of great relevance. Accordingly, we have investigated the influence of the temperature on the catalytic activity of complex **2a**. As seen in Table 4, when the reaction was carried out at 20 °C in toluene, the yield of product was 26%, at 60 °C the yield of product was improved to 68%, and what is more important, only traces of biphenyl were detected by ^1H NMR analysis of the crude reaction mixture. A temperature of 80 °C was required to reach a reasonable reaction speed (entry 5), although 74% yield was obtained at 3 h, reaction went to completion (85% yield) within 5 h.

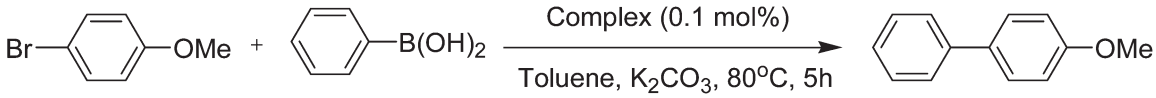
Table 5 The effect of a low loading of catalyst on Suzuki coupling[a]



Entry	Mol% Pd	Yield (%)[b]	TON (mol product/mol cat)
1	10^{-1}	85	850
2	10^{-2}	83	8300
3	10^{-3}	78	78 000
4	10^{-4}	69	690 000
5	10^{-5}	12	1 200 000

[a] Conditions: 4-bromoanisole (2.0 mmol), phenylboronic acid (3.0 mmol), complex **2a**, K_2CO_3 (4.0 mmol), toluene (20 ml), 80 °C, 5 h. [b] Isolated yields.

Table 6 Effect of the catalyst on Suzuki coupling[a]



Entry	Complex	Yield (%)[b]
1	2a	85
2	2b	87
3	2c	88
4	2d	92

[a] Conditions: 4-bromoanisole (2.0 mmol), phenylboronic acid (3.0 mmol), 0.1 mol%, K_2CO_3 (4.0 mmol), toluene (20 ml), 80 °C, 5 h. [b] Isolated yields.

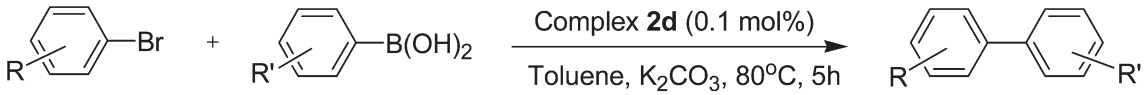
Low catalyst loading tests were performed in order to find out the efficiency of the catalyst. In order to optimise the reaction conditions, different catalyst : substrate (C : S) ratios were tested in toluene and K_2CO_3 and the results are summarised in Table 5. The coupling reaction carried out between 4-bromoanisole and phenylboronic acid using a C : S ratio of 1 : 1000 proceeded to completion with an 85% yield (entry 1). When increasing the C : S ratio to 1 : 10 000 and 1 : 100 000, the reaction still proceeds smoothly, accompanied by a drop in yield. Interestingly, these reactions could also be conducted with an ultra-low loading of catalyst as low as 0.00001 mol%, with high turnover numbers. Thus, it was concluded that a catalyst : substrate ratio of 1 : 1000 is the best compromise between the optimum reaction rate and S : C ratio in toluene.

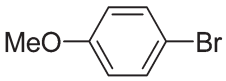
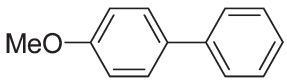
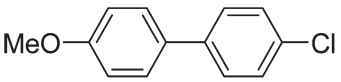
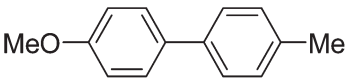
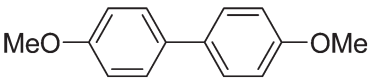
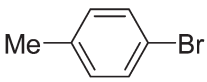
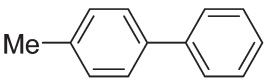
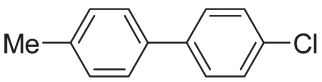
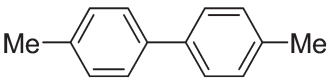
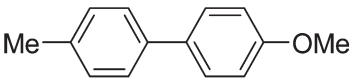
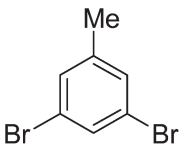
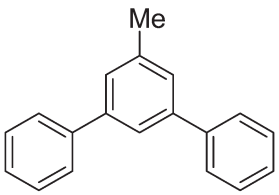
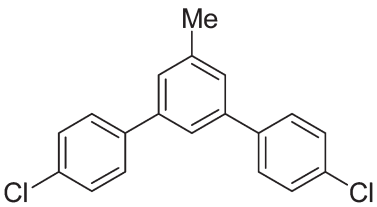
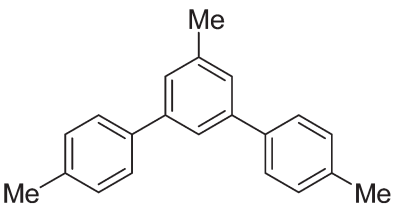
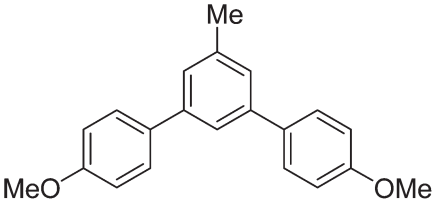
We further examined the effect on performance of changing the R substituents on the thiocarboxamide coordinated to palladium. To this purpose, we have studied the catalytic activities of all complexes **2a–d** in the coupling reaction using a C : S ratio of 1 : 1000 and it was observed that the complex **2d** showed increased yields of the cross coupled products (Table 6). The substitution of a pyridyl group at the terminal nitrogen of the coordinated ligand and the planarity of complex **2d** may be responsible for its observed excellent catalytic activity over the other three complexes. Using the complex **2d**, Suzuki coupling of a series of arylbromides with different arylboronic acids has been carried out under optimised conditions (Table 7). In the case of *p*-methoxyboronic acid the conversion to biaryls was 96% (entry 4), which takes place at a faster rate than that of *p*-methylboronic acid (93%). The presence of the electron withdrawing (Cl) substituent on boronic acids has a significant effect on the conversion to their corresponding biaryls. Similar observations are also made in the case of triaryls. The *p*-bromoanisole gave high conversions compared to other arylbromides.

Pyridines are the most common heterocyclic motif found in pharmaceutically active compounds.[40] Thus, preparative methods for pyridine derivatives remain an essential research topic in organic synthesis. Despite efforts by numerous groups, pyridine-derived bromides have been proved to be a particularly difficult class of substrate for the Suzuki reaction.[41] The cross coupling of heteroaryl bromides using the same complex **2d** has been performed and the results are summarised (Table 8). Interestingly, these reactions could also be conducted with low loading of catalyst (0.1 mol%). Heteroaryl bromides afforded almost quantitative yields of products. Substituted-2-bromopyridine underwent a smooth reaction with phenylboronic acid, providing a useful way for the synthesis of aryl-substituted nitrogen heterocycles. These results indicate that with these α-substituted heteroaryl bromides, a possible interaction between the heteroelement and the palladium complex has a deactivation effect on the rate of the reaction.

To monitor the recyclability of this catalytic system similar reaction conditions with 0.1 mol% catalyst were employed. We have observed some Pd blacks after each run and the catalyst was completely deactivated after the fourth run. For weak bases such as NaOAc, NEt_3 deactivation occurred more slowly than for strong bases. The first reaction afforded the corresponding

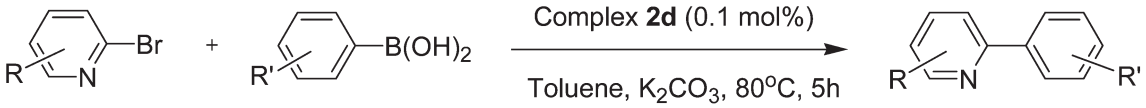
Table 7 Suzuki coupling of aryl bromides with aryl boronic acids[a]

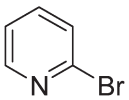
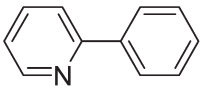
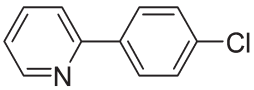
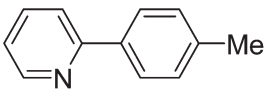
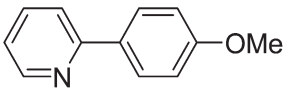
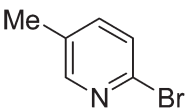
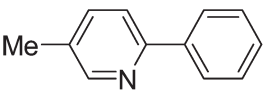
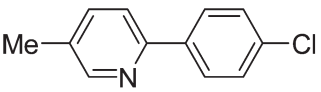
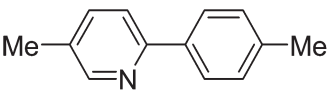
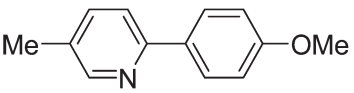
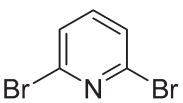
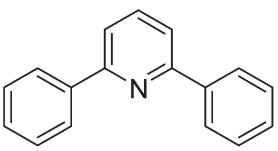
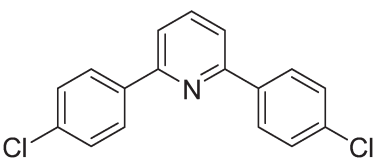
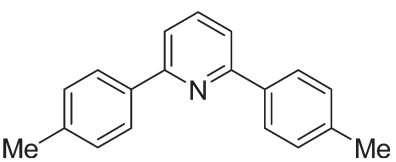
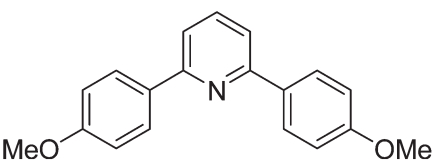


Entry	Aryl bromide	Arylboronic acid (R′)	Product	Yield (%)[b]
1		H		92
2		Cl		87
3		Me		93
4		OMe		96
5		H		81
6		Cl		78
7		Me		86
8		OMe		94
9		H		78[c]
10		Cl		74[c]
11		Me		83[c]
12		OMe		93[c]

[a] Conditions: aryl bromide (2.0 mmol), arylboronic acid (3.0 mmol), 0.1 mol% **2d**, K_2CO_3 (4.0 mmol), toluene (20 ml), 80 °C, 5 h. [b] Isolated yields. [c] Double Suzuki cross coupling (aryl bromide (2.0 mmol), arylboronic acid (6.0 mmol), 0.2 mol% **2d**, K_2CO_3 (8.0 mmol) were used).

Table 8 Suzuki coupling of heteroaryl bromides with aryl boronic acids[a]



Entry	Heteroaryl bromide	Arylboronic acid (R′)	Product	Yield (%)[b]
1		H		82
2		Cl		79
3		Me		88
4		OMe		94
5		H		78
6		Cl		74
7		Me		86
8		OMe		95
9		H		73[c]
10		Cl		71[c]
11		Me		82[c]
12		OMe		90[c]

[a] Conditions: heteroaryl bromide (2.0 mmol), arylboronic acid (3.0 mmol), 0.1 mol% **2d**, K_2CO_3 (4.0 mmol), toluene (20 ml), 80 °C, 5 h. [b] Isolated yields. [c] Double Suzuki cross coupling (heteroaryl bromide (2.0 mmol), arylboronic acid (6.0 mmol), 0.2 mol% **2d**, K_2CO_3 (8.0 mmol) were used).

coupling product in 92% yield, the product yield for the second cycle was nearly the same (86%), however in the third cycle it was 72% and it was reduced to 49% which was obtained after the fourth run although more time was taken (8–10 h for each run).

Conclusions

The present work describes a simple and convenient method to synthesise a series of palladium(II) thiocarboxamide complexes incorporating triphenylphosphine. Analytical, spectral and X-ray diffraction studies reveal that the ligand coordinated to palladium *via* pyridine N and thiol S. All the complexes **2a–d** were structurally characterised by X-ray crystallography, which witnessed a square planar geometry. We have developed efficient Pd(II) catalysts for Suzuki coupling reactions under ambient conditions to couple challenging substrates like deactivated aryl and heteroaryl bromides that provides a moderate to good yield of desired products. Reactions also work with a low loading of catalyst under aerobic atmosphere for mono and double Suzuki cross coupling. Our current investigations are focused on the feasibility of electronic modification around phosphine–palladium catalysts, through phosphorus substituents, with the view to increasing their activity.

Experimental

General

All reactions were carried out under an atmosphere of air. C, H, N and S analyses were carried out with a Vario EL III CHNS elemental analyser. IR spectra were recorded on a Perkin–Elmer 597 spectrophotometer, using KBr pellets. ^{1}H NMR, ^{13}C NMR and ^{31}P NMR were conducted on a high resolution Bruker Avance 400 spectrometer, in $CDCl_3$ as solvent. Melting points were performed with an electrical instrument and are uncorrected.

The ligands **1a–d**,[32] were prepared according to literature methods. All other chemicals were used as received. Solvents were dried and freshly distilled prior to use. Toluene was distilled under nitrogen with Na-benzophenone. Column chromatography was performed on neutral silica gel.

Syntheses

General method for the synthesis of the palladium complexes. A heated solution (50 °C) of appropriate ligands (1 equiv.) in ethanol (20–30 mL) was stirred under an air atmosphere. Upon dissolution of the pyridine-2-thiocarboxamide in ethanol, $PdCl_2(PPh_3)_2$ (1 equiv.) was added and the resultant mixture was then heated to reflux temperature for 3 h, then allowed to cool to room temperature. The orange precipitate was filtered, washed with ethanol and dried *in vacuo* to give moderate to good yields. All the complexes were highly soluble in MeOH, CH_2Cl_2, $CHCl_3$ and acetone.

[Pd(Cl)(κ^2-*S*,*N*-C_6H_4CS=N-(2-ClPh)(PPh_3)], 2a. Yield 66%. M.p. 197 °C (with decomposition). Found: C, 55.09; H, 3.54; N, 4.28; S, 4.90. Calc. for $C_{30}H_{23}Cl_2N_2PPdS$: C, 55.27; H, 3.56; N, 4.30; S, 4.92%. IR (KBr) $\bar{\nu}$ = 1562(m), 1281(s) cm^{-1}. NMR ($CDCl_3$): δ_H (400 MHz) 9.58 (d, 1H, C-1), 7.65–7.25 (m, 23H, Ar, PPh_3) ppm. δ_C (100 MHz) 160.02, 149.62, 146.94, 138.81, 134.76, 134.65, 132.16, 132.06, 131.98, 131.16, 129.56, 129.30, 128.74, 128.59, 128.46, 128.25, 128.14, 126.42, 126.03, 124.72, 123.64, 121.44 ppm. δ_P (160 MHz) 30.76 ppm.

[Pd(Cl)(κ^2-*S*,*N*-C_6H_4CS=N-(2-MePh)(PPh_3)], 2b. Yield 74%. M.p. 201 °C (with decomposition). Found: C, 58.81; H, 4.17; N, 4.46; S, 5.05. Calc. for $C_{31}H_{26}ClN_2PPdS$: C, 58.96; H, 4.15; N, 4.44; S, 5.08%. IR (KBr) $\bar{\nu}$ = 1545(m), 1275(s) cm^{-1}. NMR ($CDCl_3$): δ_H (400 MHz) 9.58 (t, 1H, C-1), 7.93–6.86 (m, 23H, Ar, PPh_3), 2.10 (s, 3H, CH_3) ppm. δ_C (100 MHz) 160.36, 149.57, 148.34, 138.83, 134.75, 134.64, 134.14, 130.10, 129.40, 129.34, 128.25, 128.13, 126.08, 125.52, 123.98, 123.39, 119.31, 19.99 ppm. δ_P (160 MHz) 31.03 ppm.

[Pd(Cl)(κ^2-*S*,*N*-C_6H_4CS=N-(4-MePh)(PPh_3)], 2c. Yield 91%. M.p. 195 °C (with decomposition). Found: C, 59.10; H, 4.18; N, 4.42; S, 5.09. Calc. for $C_{31}H_{26}ClN_2PPdS$: C, 58.96; H, 4.15; N, 4.44; S, 5.08%. IR (KBr) $\bar{\nu}$ = 1549(m), 1267(s) cm^{-1}. NMR ($CDCl_3$): δ_H (400 MHz) 9.79 (t, 1H, C-1), 7.89–6.99 (m, 23H, Ar, PPh_3), 2.25 (s, 3H, CH_3) ppm. δ_C (100 MHz) 159.29, 148.52, 147.26, 137.55, 133.69, 133.58, 130.08, 130.05, 129.03, 128.33, 128.29, 127.77, 127.18, 127.07, 125.00, 124.46, 122.92, 122.33, 118.25, 20.92 ppm. δ_P (160 MHz) 30.92 ppm.

[Pd(Cl)(κ^2-*S*,*N*-C_6H_4CS=N-(4-Py)(PPh_3)], 2d. Yield 72%. M.p. 206 °C (with decomposition). Found: C, 56.17; H, 3.72; N, 6.76; S, 5.18. Calc. for $C_{29}H_{23}ClN_3PPdS$: C, 56.32; H, 3.75; N, 6.79; S, 5.18%. IR (KBr) $\bar{\nu}$ = 1553(m), 1277(s) cm^{-1}. NMR ($CDCl_3$): δ_H (400 MHz) 9.59 (t, 1H, C-1), 8.34–6.85 (m, 23H, Ar, PPh_3) ppm. δ_C (100 MHz) 149.64, 138.61, 134.74, 134.69, 134.63, 134.58, 132.06, 131.13, 131.01, 130.98, 129.46, 128.91, 128.23, 128.17, 128.11, 128.05, 126.17, 126.02, 123.23, 121.42 ppm. δ_P (160 MHz) 30.59 ppm.

Catalysis

General method for the Suzuki coupling of aryl and heteroaryl bromides with arylboronic acid (Tables 7 and 8). To a mixture of arylbromide (2.0 mmol), arylboronic acid (3.0 mmol) and K_2CO_3 (4.0 mmol) in toluene (20 mL) was added the catalyst (0.1 mol%) as a toluene solution (1.00 mL) made up to the correct concentration by multiple volumetric dilutions of a stock solution. The resultant mixture was then heated at 80 °C for 5 h. At ambient temperature, H_2O (10 ml) was added and the organic layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were concentrated *in vacuo* and the remaining residue was purified by Column chromatography (*n*-hexane–EtOAc: 200 : 1) to yield a colorless solid.

Recycling of the catalyst

To a mixture of 4-bromoanisole (2.0 mmol) and phenylboronic acid (3.0 mmol) was added catalyst (0.1 mol%) in toluene (20 mL) at 80 °C in the presence of K_2CO_3 (4.0 mmol). Each time, after completion of the reaction, the catalyst was recovered by centrifugation and then washed thoroughly with toluene

Table 9 Crystal data and structure refinement parameters for complexes **2a–d**

Complex	**2a**	**2b**	**2c**	**2d**
Empirical formula	$C_{30}H_{23}Cl_2N_2PPdS$	$C_{31}H_{26}ClN_2PPdS$	$C_{31}H_{26}ClN_2PPdS$	$C_{29}H_{23}ClN_3PPdS$
Formula weight	651.83	631.42	631.42	618.38
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073
Crystal system	Orthorhombic	Monoclinic	Monoclinic	Orthorhombic
Space group	*Pbca*	*C*2/*c*	*C*2/*c*	*P*2(1)2(1)2(1)
a (Å)	9.0407(2)	25.1402(9)	24.5145(4)	14.205(5)
b (Å)	14.913(3)	10.2928(3)	10.6055(1)	9.867(5)
c (Å)	40.8653(7)	23.0874(9)	23.0862(4)	19.274(5)
α (°)	90	90	90	90
β (°)	90	108.072(3)	109.559(1)	90
γ (°)	90	90	90	90
V (Å^3)	5509.62(19)	5679.4(3)	5655.81(14)	2701.5(18)
Z	8	8	8	4
D_{calcd} (Mg m^{-3})	1.572	1.477	1.483	1.520
μ /(mm^{-1})	1.025	0.900	0.904	0.946
F(000)	2624	2560	2560	3120
Crystal size (mm^3)	0.11 × 0.09 × 0.04	0.11 × 0.10 × 0.08	0.07 × 0.06 × 0.05	0.06 × 0.06 × 0.05
Theta range for data collection(°)	1.00 to 25.00	1.70 to 26.00	1.76 to 25.00	1.78 to 29.64
Index ranges	−10 < = h < = 10, −17 < = k < = 17, −48 < = l < = 48	−30 < = h < = 30, −12 < = k < = 12, −28 < = l < = 28	−29 < = h < = 29, −12 < = k < = 12, −27 < = l < = 27	−19 < = h < = 19, −13 < = k < = 13, −26 < = l < = 25
Reflections collected	47 858	49 049	43 972	43 829
Independent reflection	4845	5594	4988	7251
Max and min transmission	0.9602, 0.8956	0.9315, 0.9075	0.9465, 0.9262	0.9883, 0.9860
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	4845/0/334	5594/0/335	4988/0/335	7251/0/325
Goodness-of-fit on F^2	1.216	1.055	1.106	0.912
Final *R* indices [$I > 2\sigma(I)$] R_1, wR_2	0.0296, 0.0624	0.029, 0.0557	0.0306, 0.0698	0.0477, 0.1023
R indices(all data)R_1, wR_2	0.0355, 0.0691	0.029, 0.0606	0.0402, 0.075	0.0950, 0.1238
R(int)	0.032	0.0314	0.0387	0.202
Flack parameter	—	—	—	−0.06(4)
Largest diff. peak and hole (e Å^{-3})	0.315 and −0.301	0.343 and −0.222	0.321 and −0.342	0.746 and −1.178

followed by copious amounts of water to remove the base present in the used catalyst and finally by dichloromethane. The recovered catalyst was dried under vacuum at 105–115 °C overnight. This used catalyst was re-employed in four successive cycles under identical conditions. The combined organic layers were concentrated *in vacuo* and the remaining residue was purified by column chromatography (*n*-hexane–EtOAc: 200 : 1) to yield a colorless solid.

X-Ray structure determinations

Single crystals of all the complexes were grown by slow evaporation of dichloromethane–ethanol mixture at room temperature. A single crystal of suitable size was covered with Paratone oil, mounted on the top of a glass fiber, and transferred to a Bruker SMART APEX II single crystal X-ray diffractometer using monochromated Mo-Kα radiation (*kI* = 0.71073 Å). Data were collected at 293 K. The structure was refined by full matrix least-squares method on F^2 with SHELXL-97. Non-hydrogen atoms were refined with anisotropy thermal parameters. All hydrogen atoms were geometrically fixed and allowed to refine using a riding model. Frame integration and data reduction were performed using the Bruker SAINT-Plus (Version 7.06a) software. The multi-scan absorption corrections were applied to the data using SADABS software. Crystal data for the structures are given in Table 9.

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