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Oxazoline Chemistry. Part 11: Syntheses of natural and synthetic isoflavones, stilbenes and related species via C–C bond formation promoted by a Pd–oxazoline complex☆

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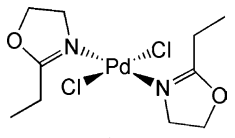
Abstract—The complex *trans*-[$PdCl_2$(2-ethyl-2-oxazoline-κ^1N)$_2$] (**1**) is shown to be an active and oxidatively robust catalyst for C–C bond forming reactions (Heck, Sonogashira, Ullmann, Miyaura–Suzuki, etc.). These reactions can be carried out in air without rigorous solvent/substrate purification and in the absence of additional free ligand. The general methodology described above has been applied to the high yield and regio-selective formation, via Miyaura–Suzuki coupling, of natural and synthetic isoflavones (i.e., isoflavone, 2′-methylisoflavone [**7b**], 3′-methylisoflavone [**7c**] and 3′,4′-benzoisoflavone: [**7d**]). Compounds **7c** and **7d** are previously unknown. In addition, the synthesis of (*E*)-tris-*O*-methylresveratrol and (*E*)-3,5-dimethoxystilbene is also described; the former is a recognized anti-cancer agent while the latter is a biologically active extract from the bark of the conifer species *Pinus armandii*. Both of these latter products are produced as a result of a Heck coupling reaction promoted by **1**.

1. Introduction

The creation of a bond between two carbon atoms is a central theme in organic chemistry. In the last 40 years, commodity chemical syntheses have increasingly relied on transition metal complexes as mediators of C–C bond formation in, for example, the catalytic hydroformylation or polymerisation of olefins.[1] In fine chemical syntheses, palladium complexes are quickly taking on a central role in such chemistry and currently a wide variety of Pd compounds are known to be useful for regio- and enantio-selective (catalytic) C–C bond formation.[1,2] These reactions are typically facilitated by Pd (pseudo-) halide complexes, which incorporate other metal binding agents, of which phosphine (i.e., PR_3), carbene and *N*-donor ligands are the most common.[1,2] One of the few drawbacks to the industrial application of a majority of these Pd derivatives is the air-sensitive nature of the active species and/or catalytic reaction intermediates, which are likely Pd(0) complexes. A further recurring problem is the potential for oxidation of 'free' ligands (e.g., PR_3) that are formed following a dissociation step in the catalytic cycle. Hence, inert atmosphere conditions are often necessary for efficient catalysis. In some cases, it is also necessary to add quantities of free ligand to stabilize the Pd during the reaction; this situation can hamper later product purification.[1,2] Therefore, there is still a need for new and oxidatively robust Pd-based systems for applications in synthetic organic chemistry.[3] Recently, we briefly communicated[4] the synthesis and use of *trans*-[bis-(2-ethyl-2-oxazoline-κ^1N) palladium(II) dichloride] (Fig. 1: complex **1**) as a promoter of C–C bond formation (Heck, Ullmann, Miyaura–Suzuki reactions, etc.).



1

Figure 1.

Compound **1** can efficiently operate in open air and does not require addition ligand (i.e., 2-ethyl-2-oxazoline: Etox) to be added to the reaction mixtures to give adequate product yields. In this report, we expand our preliminary

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Table 1. Catalysis results using complex **1** as mediator of C–C bond formation[a]

Entry	Aryl-X	Substrate	Product	Time (h)	Yield (%)	TON
1	PhI	Styrene	*t*-Stilbene	48	87	860
2	PhI	Styrene	*t*-Stilbene	24	84	1700
3	PhI	Styrene	*t*-Stilbene	18	77	2000
4[b]	PhI	Styrene	*t*-Stilbene	18	71	1900
5	*p*NO_2PhI	Styrene	*t*-NO_2-stilbene	24	>99	>2000
6	PhBr	Styrene	*t*-Stilbene	24	77	1500
7	*p*BrAn	Styrene	*t*-MeO-stilbene	24	65	1300
8	PhBr	PhBR_2	Biphenyl	3	>99	>1300
9	*p*BrAn	PhBR_2	*p*PhAn	3	>99	>1300
10	PhI	PhI	Biphenyl	3	45	11
11	PhI	PhC≡CH	PhC≡CPh	3	32	190
12[c,d]	**6a**	**6b**	**5b**	48	14	<1
13[c,d]	**6a**	Styrene	**5c**	48	22	<1
14[e]	**8a**	(2-Napthyl)BR_2	**7d**	24	60	0.83
15[e]	**8b**	(2-Napthyl)BR_2	**7d**	24	45	0.6
16[e]	**8b**	PhBR_2	**7a**	24	>99	>1.4
17[e]	**8b**	(*o*MePh)BR_2	**7b**	24	>99	>1.4
18[e]	**8b**	(*m*MePh)BR_2	**7c**	24	>99	>1.4

[a] Experimental details are given in the Section 3. TON, average turn over number per hour; Ph, phenyl; *t*-stilbene, (*E*)-stilbene; *p*NO_2PhI, 4-nitroiodobenzene; *p*BrAn, 4-bromoanisole; *p*PhAn, 4-methoxybiphenyl; *t*-NO_2-stilbene, (*E*)-4-nitrostilbene; *t*-MeO-stilbene, (*E*)-4-methoxystilbene; BR_2, B$(OH)_2$.
[b] Compound **1** (5.3 mmol) used.
[c] Ar-X (5 mmol); 6 mmol olefin; 10 mol% of **1** used.
[d] See Figure 2.
[e] See Eq. 1.

communication and detail the use of **1** for the selective formation of C–C bonds. In turn, this technology is applied to the synthesis of a number of biologically relevant isoflavone and stilbene derivatives.[5]

2. Results and discussion

The synthesis of air-stable [$PdCl_2$(Etox)$_2$] (**1**: Fig. 1) is a straightforward procedure[4] involving the treatment of methanolic solutions of Li_2PdCl_4 with Etox; this latter reagent is an inexpensive and commercially available polymer precursor.[12] Analyses of **1** via single crystal X-ray diffraction[4] has revealed that it exists as the trans-isomer in the solid-state and presumably only the trans form is present in any detectable amount (NMR) in solution.[†] As expected, the oxazoline ligands are found to coordinate through the *N*-donor atom.[13] There are only a few reported structural analogues of **1** in the literature.[14–16] The complex *trans*-[$PdCl_2$(2-phenyl-2-oxazoline-κ^1N)$_2$] (**2**) has been described by Dunina et al.;[14] a related naphthalene compound has also been reported[15] by van Koten's group (viz., *trans*-[$PdCl_2$(4,4-dimethyl-2-{2′-napthyl}-2-oxazoline-κ^1N)$_2$]: **3**). Complex **3** exists as a mixture of cis and trans isomers in solution,[15] although in the solid phase only the trans form is found. This is in contrast to our recent NMR observations of **1**[4] and earlier independent studies of **2**.[14] A structurally analogous oxazole complex, *trans*-[$PdCl_2$(2-oxazole-κ^1N)$_2$] (**4**), has also been reported.[16] No evidence for isomerisation of this material was noted. The catalytic potentials of **2**–**4** do not appear to have been investigated.[14–16]

Our interests are centred on the synthesis,[17] coordination[2a,4,18] and medicinal inorganic chemistry of 2-oxazolines (i.e., 4,5-dihydro-2-oxazoles) and the application of such complexes in catalysis.[2a,4] One of our objectives is to design robust materials for use in catalysis under non-inert atmosphere conditions. We therefore tested solutions of **1** for its catalytic potential under standard bench-top conditions in open air. No free ligand was added to the reaction mixtures. Palladium complexes[1–3] are typically tested on a single class of C–C bond forming reaction (e.g., for Heck coupling). We have found that **1** can be used for a variety of such processes (Table 1) including the Heck (entries 1–7, 12 and 13), Miyaura–Suzuki (entries 8–9 and 14–18), Ullmann (entry 10) and Sonogashira (entry 11) coupling reactions under typical conditions.[1–3]

Complex **1** is an effective catalyst for all of these classes of C–C bond forming reactions although turnover numbers are admittedly moderate. There are few fully characterised (pre-formed) Pd-based systems that have been shown to be effective for a plethora of different C–C bond forming processes and even fewer that can operate in air and without additional ligand.[1–3] This system effectively combines these two aspects with the further advantage of using a simple, very inexpensive (or readily synthesised) and air-stable ligand. Etox, like most oxazolines, is very stable to oxidative decomposition. This aspect gives a clear advantage over the use of air-sensitive phosphine and carbene ligands.

Unfortunately, the main disadvantage with this system is that aryl-chlorides are not activated to any significant extent by **1**. Our tests with this complex (in air) under the standard Heck conditions using a combination of PhCl and styrene as substrates gave no evidence for the formation of the desired stilbene product. In addition, **1** is ineffective as a catalyst for the Sonogashira reaction in the absence of CuI (yields <10%). The use of pyrrolidine as solvent is also crucial for Sonogashira coupling as reactions performed in refluxing toluene or NEt_3 gave no coupled product; likewise only a trace of product (~1%) was found using DMF as reaction

[†] We have previously disclosed[4] the full experimental details of the synthesis and characterisation (NMR, X-ray, etc.) of **1**.

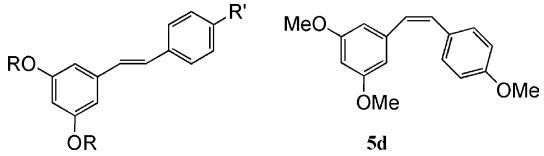
medium. Not surprisingly, 1,4-dihydroquinone was found to be essential for the Ullmann coupling.

A further observation is that **1** does not promote the Stille reaction.[1,2] Our examination of this process involved using **1** in the presence of PhI or *p*-bromoacetophenone in combination with either $R_3SnC_6H_5$ or $R_3SnCH_2CH{=}CH_2$ (R = *n*-Bu; conditions: toluene, 100 °C, 8 h). These experiments yielded no detectable (coupled) product[4] and hence further Stille-type reactions were not attempted.

The Heck reaction was used as a means to further explore the effects of temperature, the nature of base, solvent, substrate and added free ligand to the overall yield of stilbene product. The use of aryl-halides with electron-withdrawing groups appears to enhance the yields of coupled product (Table 1; entries 3 and 5), whereas electron-donating groups give the opposite effect (Table 1; entries 6 and 7). Adjusting the nature of added base from sodium acetate to potassium carbonate or to NEt_3 had no effect on the overall yield of product nor did changing the solvent from DMF to NEt_3. However, the addition of five-fold excess of free ligand (Etox) reduced the overall yield to only 25% under identical conditions. This strongly suggests that dissociation of one or more equivalents of Etox is a key component of the rate determining step(s) during catalysis.[‡] The importance of (formally) 14-(valence metal) electron intermediates, for example, $[PdCl_2(Etox)]$, have been proposed previously in related Heck systems[1,2] and may also be important here. There is a pronounced temperature effect on this reaction; adjusting the bath temperature from 140 to 120 °C leads to greatly reduced yields (25%). Running the reaction at even lower temperature (100 °C) gives only a trace (7%) of product stilbene.

Having established some of the limitations and potential of **1** in C–C coupling chemistry,[4] we felt that this technology would be more useful if it can be shown to produce more elaborate and/or desirable organic products.

Many (substituted) (*E*)-stilbenes (i.e., derivatives of stilbene itself) can be extracted from natural sources.[5b,19] In particular, resveratrol (**5a**) and its tris-*O*-Me analogue (**5b**: Fig. 2) have been of recent interest due to the health benefits that are attributed to consumption of such compounds by mammalian organisms. Resveratrol is a component of many red wines[20] and it has been linked as a possible causative agent of the so-called 'French paradox'. This involves the statistical fact that the intake of high fat foods, which is common in the diet of French citizens, does not result in a significant increase in heart disease or other aliments within the general population.[21] For this and other reasons, **5a** and its analogues are currently at the centre of considerable scrutiny within medicinal chemistry. A key component in a retro-synthetic pathway to **5a** is **5b**, which upon methyl–proton exchange obviously yields **5a**.[8] Compound **5b** is of interest in its own right due of its documented anti-cancer properties and because it is a key precursor to its (*Z*)-isomer **5d** (Fig. 2), which has been shown to be a more effective anti-cancer agent then resveratrol itself.[22] The related stilbene **5c** (Fig. 2), isolated from the bark of the conifer species *Pinus armandii*,[9] has also been investigated for its medicinal properties.[23] We therefore choose to target **5b** and **5c** for synthesis using **1**. Previously reported routes to these two compounds have included multi-step Wittig and/or McMurray reactions[23] and the Perkin reaction.[19] Palladium-catalysed Heck reactions[24a] have also been used; this can involve the use of acetate protected 5-vinylresorcinol (produced in five steps), vinylsilanes as the olefin source[24b] or other substrates.[3k,25] We decided to investigate the use of **1** as a mediator of C–C coupling to yield **5b** or **5c** using commercially available organic precursors: viz. 3,5-dimethoxy-1-bromobenzene (**6a**) combined with either 4-vinylanisole (**6b**: for the synthesis of **5b**) or styrene (for **5c**). Thus, treatment of solutions **6a** and **6b**, under conditions as described in Table 1 (Entry 12 and the Section 3), produced **5b** in a poor isolated yield of only 14%. In turn, the treatment of **6a** with styrene, under similar conditions, led to the isolation of **5c** (22% yield: Table 1; entry 13). These two syntheses, with reduced yields versus that of stilbene itself (vide supra), support the previous observations that electron-donating groups (Table 1) on the haloarene substrate lead to a reduction of the rate and/or efficiency of Heck coupling. This may be due to an unusually stable aryl-Pd complex formed during the catalytic cycle[1–3] and hence base promoted reductive elimination of the desired stilbene is sluggish.[3w,‡] Thus, yields are unimpressive of these two products. However, these reactions do represent a facile alternative strategy for the synthesis of **5b** and **5c** that employs simple (commercial) organic starting materials and an easily produced catalyst precursor.



5a: R = H, R' = OH;
5b: R = Me, R' = OMe;
5c: R = Me, R' = H

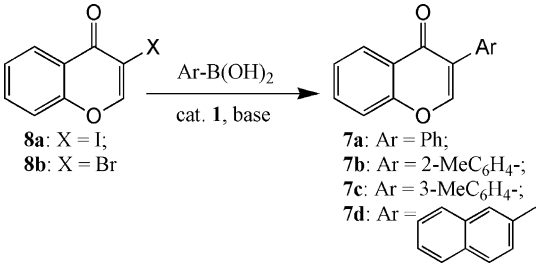
5d

Figure 2.

A survey of entries 1–13 in Table 1 reveals that of all the types of C–C coupling that we have attempted, the Miyaura–Suzuki reaction is the cleanest and generally gives the best yields of coupled product. Coincidently, as part of one of our structure–activity relationship studies, we required a quantity of substituted bicyclic compounds of the isoflavone class (Eq. 1; e.g., **7a**–**7d**). These derivatives therefore presented us with a good series of candidates for our investigations of coupling chemistry using **1**. Isoflavones represent a very important class of natural products[26] because they display a wide variety of biological properties that include anti-cancer, anti-oxidant, anti-inflammatory, anti-bacterial and anti-fertility activity. In addition, isoflavones have been shown to act as selective enzyme inhibitors[5b–f,26], to alleviate erectile dysfunction[27] and have been investigated as medicinal agents for the

[‡] The effect of added free ligand is not as pronounced when using **1** to perform Miyaura–Suzuki coupling reactions. Full experimental and theoretical mechanistic investigations of these reactions will be the subject of a later publication.

treatment of alcohol addiction.[28] Our synthetic methodology revolves around the use of the readily available[6] 3-halochromones **8a** and **8b** (Eq. 1; also see Section 3) in a Miyaura–Suzuki reaction in combination with arylboronic acid derivatives.[11,29]



8a: X = I;
8b: X = Br

7a: Ar = Ph;
7b: Ar = 2-MeC_6H_4-;
7c: Ar = 3-MeC_6H_4-;
7d: Ar =

(1)

Thus, the treatment of **8a** (Table 1; entries 18) or **8b** (entries 14–17) with a variety of arylboronic acids (Eq. 1) gives excellent yields of the known isoflavones **7a** (i.e., isoflavone) and **7b** (2′-methylisoflavone) in addition to the novel compound **7c** (3′-methylisoflavone). Only in the case of previously unknown **7d** (i.e., 3′,4′-benzoisoflavone) is the yield moderate. We attribute this to steric effects of the large naphthalene group. A marginal improvement in yield could be obtained by the use of **8a** instead of the bromo analogue **8b**.

The chemistry described above has indicated that a simple and air-stable oxazoline complex can be used in several 'benchmark' C–C bond forming reactions and that such methodology can be applied to produce desirable organic products.

3. Experimental

3.1. General procedures

All reactions were carried out using standard bench-top laboratory techniques using commercially available, reagent-grade solvents. Unless otherwise stated, literature mp, IR and ^{1}H NMR data were obtained from the Aldrich Chemical Co. Catalogue (2005–2006 Ed.) and/or the Aldrich Libraries of FT-IR or FT NMR Spectra. ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded from chloroform-*d* solutions at 300 MHz using a Bruker Advance™ 300 MHz NMR spectrometer operating at room temperature (rt). Chemical shift values are reported in parts per million relative to TMS ($\delta = 0.00$ ppm) as external standard; coupling constants (*J*) are reported in Hertz. Mass spectra (MS) were obtained from the Dalhousie University Mass Spectral Facility and were performed in electron impact (EI) mode. Microanalyses were recorded at the analytical services department (ANALEST) of the University of Toronto. IR spectra were obtained as Nujol muls or as KBr disks using a Perkin Elmer 683 IR spectrometer or a Nicolet Magna 560 FT-IR spectrometer. Melting point data was obtained using a Mel-Temp II apparatus and reported values are uncorrected. The synthesis of compound **1** was carried out as described in the literature.[4] 3-(Dimethylamino)-1-(2-hydroxyphenyl)-propen-1-one and 3-bromochromone (**8a**) were produced as described by Gammill.[6] All yields in Table 1 refer to the pure (^{1}H NMR, mp, IR) products isolated by extraction and flash column chromatography and/or recrystallisation as detailed for the individual components below, unless otherwise stated.

3.2. Syntheses of *trans*-stilbene, (*E*)-4-nitrostilbene, 5b and 5c

The synthesis of these four compounds was carried out as described below for *trans*-stilbene except where noted.

3.2.1. Synthesis of *trans*-stilbene. A 25 mL quantity of DMF was added to a 50 mL round-bottomed flask. This flask was then charged with 0.00053 mmol (0.15 mg) of **1**, 25 mmol (5.1 g) of iodobenzene (or 3.9 g of bromobenzene), 30 mmol (3.1 g) of styrene and 30 mmol (2.5 g) of sodium acetate. The mixture was then heated to between 140 and 150 °C for the amount of time specified in Table 1 (entries 1–4, 6 and 8). The reaction mixture was cooled to rt and then all volatile components were evaporated in vacuo. The residue was purified by flash chromatography on silica gel (230–400 mesh) using hexanes–EtOAc (9/1) as eluent. The product *trans*-stilbene thus isolated gave a correct ^{1}H NMR spectrum and mp (and a non-depressed mixed mp) when compared to an authentic (commercial) sample.

3.2.2. Synthesis of (*E*)-4-nitrostilbene. Yield: >98% (purity: >97% [NMR]); mp 140 °C (lit.:[7a] 157 °C); correct ^{1}H NMR spectrum.[7b]

3.2.3. Synthesis of (*E*)-3,5,4′-trimethoxyresveratrol (5b). Yield: 14%; mp 52–53 °C (lit.:[8] 56–57 °C); correct IR and ^{1}H NMR spectrum.[9] A 10 mol% quantity of catalyst was used.

3.2.4. Synthesis of (*E*)-3,5-dimethoxystilbene (5c). Yield: 22%; mp 54–55 °C (lit.:[10] 54–55 °C); correct ^{1}H NMR spectrum. A 10 mol% quantity of catalyst was used.

3.3. Synthesis of biphenyl and *p*-phenylanisole via Suzuki coupling

The synthesis of these two compounds was carried out as described for biphenyl below.

3.3.1. Synthesis of biphenyl. A 2 mmol (0.31 g) quantity of bromobenzene was mixed with 4 mmol (0.56 g) of K_2CO_3, 3 mmol (0.37 g) of phenylboronic acid, 0.00053 mmol (0.15 mg) of **1** and a 10 mL quantity of toluene. The mixture was heated at 110 °C for 3 h. After the reaction mixture was cooled to rt, the volatile components were then removed (vacuo) and the crude mixture was extracted with water and EtOAc (20 mL each). The organic layer was washed with further EtOAc (2×20 mL) and the organic fractions combined, dried (Na_2SO_4), and evaporated to give the crude product. The desired compound, biphenyl (correct mp, IR and ^{1}H NMR spectrum; yield >99%), was isolated by recrystallisation from a mixture of EtOAc and hexanes.

3.3.2. Synthesis of 4-phenylanisole. Yield >99%; mp 87–88 °C (lit.: 86–90 °C).

3.4. Synthesis of biphenyl via Ullman coupling

A DMF (5 mL) solution was prepared that consisted of 2 mmol (0.41 g) of iodobenzene, 2 mmol (0.28 g) of K_2CO_3, 1 mmol (0.11 g) of 1,4-dihydroquinone, and 0.014 mmol (4 mg) of **1**. The mixture was heated at 110 °C for 3 h. Volatile components of the mixture were removed (vacuo) and the residue purified by flash column chromatography (hexanes) to yield biphenyl (45%).

3.5. Synthesis of diphenylacetylene

A 0.0011 mmol (0.4 mg) sample of **1** was added to a mixture of 2 mL pyrollidine, 2 mmol (0.41 g) iodobenzene, 1 mmol (0.19 g) of CuI and 2.4 mmol (0.25 g) of phenylacetylene in a 25 mL round-bottomed flask. The contents of the reaction vessel were then heated to 90 °C for 3 h. The volatile components were then removed (vacuo) and the crude mixture was extracted with water and EtOAc (20 mL). The aqueous layer was washed with further EtOAc (2×20 mL) and the organic fractions combined, dried ($MgSO_4$) and evaporated to give the crude product(s). The desired compound, diphenylacetylene (correct IR and ^{1}H NMR spectrum), was isolated (32%) by flash column chromatography using 9:1 hexanes/EtOAc as eluent.

3.6. Synthesis of 3-iodochromone (i.e., 3-iodo-4*H*-benzopyran-4-one: 8a)

In a modification of the synthesis of **8b**,[6] a sample (2.0 g: 11 mmol) of 3-(dimethylamino)-1-(2-hydroxyphenyl)-propen-1-one was dissolved in chloroform (20 mL) and the mixture cooled to 0 °C. A solution of I_2 (2.7 g: 22 mol) was added dropwise over a period of several minutes. The mixture is then diluted with water (20 mL) and stirred vigorously for 15 min. Excess iodine was then neutralized with aqueous $Na_2S_2O_3$. The organic layer was then separated, dried ($MgSO_4$) and then the volatile components were removed (vacuo). The crude yellow compound was purified by flash column chromatography (hexanes/EtOAc: 3:1) to give the yellow-coloured product 3-iodochromone (1.0 g: 35%); mp 87–88 °C (lit.:[9] 93–94 °C); IR, MS and ^{1}H NMR spectrum are consistent within experimental error to the known properties of **8a**.[9]

3.7. Syntheses of isoflavones 7a–7d

The synthesis of isoflavone (**7a**) is a representative example.

3.7.1. Synthesis of isoflavone (7a). A 0.112 g sample of **8b** (0.50 mmol) was dissolved in 10 mL of toluene in the presence of 0.75 mmol of phenylboronic acid (0.091 g), 1 mmol of K_2CO_3 (0.14 g) and 0.015 mmol (3 mol%: 0.0041 g) of **1**. The reaction mixture was then heated to reflux temperature for a period of 24 h; the flask was then allowed to cool to rt. Volatile components of the reaction vessel were then removed (vacuo) and the crude mixture was then partitioned between EtOAc (20 mL) and water. The aqueous layer was separated and extracted twice with EtOAc (40 mL total) and then the organic fractions were combined together, dried (Na_2SO_4), filtered and then the solvent was removed (vacuo). The residue was then subjected to separation via column chromatography (flash: SiO_2) with hexanes–EtOAc (9/1) as eluent to give the product isoflavone (**7a**: 0.11 g: >99% yield; R_f=0.52). The physical properties (mp, IR, ^{1}H NMR) of **7a** isolated in this way were fully consistent with the previously reported data.[11]

3.7.2. Synthesis of 2′-methylisoflavone (7b). Yield 0.11 g: >99% using 2-tolylboronic acid. ^{1}H and ^{13}C{^{1}H} NMR spectra were consistent with **7b**;[11] mp=112–113 °C (lit.:[11] 113.5–114 °C).

3.7.3. 3′-Methylisoflavone (7c). Yield 0.11 g: >99% using 3-tolylboronic acid. R_f=0.54 (hexanes/EtOAc: 9:1); mp=87–89 °C; IR (KBr): 1646 cm^{-1} (C=O); ^{1}H NMR: δ=2.43 (s, 3H, C*H*$_3$), 7.22 (d, 1H, J=6.6 Hz, Ar*H*), 7.34–7.50 (m, 5H, Ar*H*), 7.69 (t, 1H, J=7.2 Hz, Ar*H*), 8.02 (s, 1H, =C*H*), 8.35 (d, 1H, J=6.9 Hz, Ar*H*); ^{13}C{^{1}H} NMR: 176.4, 156.7, 153.8, 134.1, 133.8, 133.5, 129.9, 128.6, 128.4, 128.3, 128.1, 127.4, 126.9, 126.7, 125.8, 125.7, 125.1, 118.5. MS (EI, 70 eV): 236 (100%; M+: calcd: 236). Anal. Calcd for $C_{16}H_{12}O_2$ (%): C 81.34, H 5.12; found: C 80.83, H 5.12.

3.7.4. Synthesis of 3′,4′-benzoisoflavone (7d). Synthesised from 2-napthylboronic acid and **8b** (yield 45%; 0.061 g) or **8a** (yield 60%). R_f=0.47 (hexanes/EtOAc: 9:1); mp=184–186 °C; IR (KBr): 1645 cm^{-1} (C=O); ^{1}H NMR: δ=7.45–7.56 (m, 4H, Ar*H*), 7.71–7.76 (m, 2H, Ar*H*), 7.87–7.95 (m, 3H, Ar*H*), 8.08 (s, 1H, =C*H*), 8.35 (d, 1H, J=6.9 Hz, Ar*H*); ^{13}C{^{1}H} NMR: 176.9, 156.7, 153.8, 134.1, 133.8, 133.5, 129.9, 128.6, 128.4, 128.3, 128.1, 127.4, 126.9, 126.7, 125.8, 125.7, 125.1, 118.5. MS (EI, 70 eV): 272 (60%; M+: calcd: 272). Anal. Calcd for $C_{19}H_{12}O_2\cdot H_2O$ (%): C 81.12, H 4.66; found: C 81.13, H 4.61.

4. Conclusions

In conclusion, Pd complex **1** has been found to be an effective catalyst, in open air, for a number of C–C bond forming reactions; this compound can be used for the synthesis of pharmaceutically relevant isoflavones and stilbenes. These results suggest that simple oxazoline–Pd complexes should be further investigated for their potential applications in catalysis. Complex **1** is best suited for Miyaura–Suzuki coupling reactions and is somewhat sluggish for the Heck, Ullmann and Sonogashira processes. Stille-type coupling reactions are not catalysed by **1** (in open air). We are currently expanding this chemistry to include enantio-selective substrate activation using chiral oxazoline ligands; the investigation of the mechanism of reactions mediated by **1** and its (chiral) analogues will be disclosed in a future publication.

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