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Bis(triphenylphosphine)palladium(II)succinimide as a precatalyst for Suzuki cross-coupling—subtle effects exerted by the succinimide ligand

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Abstract—A new palladium(II) precatalyst for Suzuki cross-coupling of aryl halides and organoboronic acids has been identified, namely bis(triphenylphosphine)palladium(II)succinimide [$(Ph_3P)_2Pd(N\text{-}Succ)_2$] **2**. The precatalyst is easily prepared from palladium(0) precursors, such as $(Ph_3P)_4Pd$ or $Pd_2dba_3{\cdot}CHCl_3/Ph_3P$ and succinimide, is air, light and moisture stable, and may be employed with a variety of substrates to give the cross-coupled products, in good yields and in reasonable time, at relatively low catalyst loadings.

Palladium-catalysed reactions constitute some of the most important transformations available to the synthetic chemist.[1] Since the early 1970's, many different types of carbon–carbon and carbon-heteroatom forming bond technologies have been developed, such as the Hartwig–Buchwald,[2] Heck,[3] Negishi,[4] Sonogashira,[5] Stille[6] and Suzuki[7] cross-coupling processes. The latter reaction, where organohalides react with organoboronic acids in the presence of base and a Pd(0) catalyst, or a Pd(II) precatalyst, arguably represents one of the most applied reactions in academia and industry (Eq. 1). It is for this reason that Suzuki cross-coupling has become the benchmark by which new catalysts/precatalysts are most commonly evaluated. Highly active Pd-catalysts for this reaction have been recently developed by a number of research groups.[8] The differences between these catalysts most often arises through changes in the coordinating ligand, that is, use of electron rich alkyl phosphines, such as $(t\text{-Bu})_3P$ or biphenyl$(t\text{-Bu})_2P$, *N*-heterocyclic carbenes or phosphinites. The electronic and steric properties of these ligands are clearly important in tuning the catalytic properties of the palladium centre. Somewhat surprisingly the role of the halide ligand[9] in palladium(II) precatalysts has generally been ignored, and it has been questioned whether there is the possibility that alteration of this ligand might change the catalytic properties of the palladium centre. Studies by Amatore and Jutand have demonstrated that halide ligands from Pd(II) precatalysts are likely to play a role with the catalytic cycle—anionic Pd(0) species containing one halide ligand, of the type $[L_2Pd(0)X]^-$ ($L{=}R_3P$), are considered important.[10] This has led us to systematically investigate the importance of halides and pseudohalides in several Pd-catalysed cross-coupling reactions.

$$R{-}X + R'{-}B(OH)_2 \xrightarrow[\text{Base}]{[\text{Pd}]} R{-}R' \qquad (1)$$

The incorporation of hemilabile imidate ligands, such as succinimide, maleimide and phthalimide with palladium would allow us to determine whether pseudohalides effect the palladium centre.[11] Imidate ligands have been described as pseudohalides, exerting unusual, but potentially exploitable effects for metal centres.[12] The hemilability of imidate ligands derives from their ability to act as either monodentate or bidentate ligands. Generally four coordination modes to transition metals are considered possible (**I-IV**, Fig. 1).

These interesting modes of coordination[13] might offer unique stabilizing properties for key catalytic intermediates. To this end, we have previously shown that the Stille cross-coupling reaction is promoted by succinimido based Pd(II)

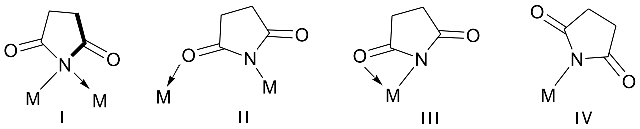

Figure 1. Possible coordination modes of succinimide ligands to metal centres.

Keywords: Suzuki cross-coupling; Biaryls; Palladium; Succinimide.

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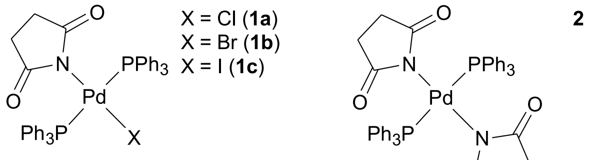
precatalysts (**1a**-**c**, Scheme 1), resulting in improved isolated yields of the products, as well as showing remarkable substrate selectivity.[14]



Scheme 1. General Suzuki cross-coupling reaction; known precatalysts **1a**-**c** and the novel precatalyst **2**.

In preliminary studies, we have further established that precatalyst **1b** is able to catalyze the Suzuki cross-coupling reaction of 4-nitro-bromobenzene and phenylboronic acid to give the cross-coupled product in good yield (74%), although 5 mol% of precatalyst is required. Lower catalyst loadings (0.5 mol%) gave incomplete conversion to products (~55%). In an effort to improve on these conversions and subsequent isolated yields, and to reduce the catalyst loading, we turned our attention to the related Pd(II)-complexes, containing two succinimide ligands.

The oxidative addition of succinimide to $(Ph_3P)_4Pt$ and $(Ph_3P)_4Pd$, to give $(Ph_3P)_2Pt$(*N*-Succ)H and $(Ph_3P)_2Pd$(*N*-Succ)$_2$ **2**, respectively, has been described by Roundhill.[15] However, detailed structural information on **2** is very limited. Using a modified procedure (method A) to that reported, we found that $(Ph_3P)_4Pd$ reacted with 2 equiv. of succinimide in benzene at 25 °C after 12 h to give the *trans*-complex **2** in 87% yield. We were further able to access **2** starting from $Pd_2dba_3{\cdot}CHCl_3$ (dba=dibenzylidene acetone), by initial reaction with Ph_3P (Pd:Ph_3P, 1:2), generating a bis-ligated palladium(0) species '$(Ph_3P)_2Pd$-η^2-dba',[16] to give **2** in a slightly lower 73% yield (method B). The ^{31}P NMR spectrum of **2** in $CDCl_3$ exhibits one singlet at δ 20.42, however the geometry around the palladium centre cannot be confirmed by this, as the phosphorus signal for both the *cis* and *trans* isomers would be expected to appear as a singlet due to symmetry. The succinimide protons are shielded, appearing at δ 1.40 (^1H NMR). The shielding effects are presumably derived from π-stacking interactions between the carbonyl and phosphorus aromatic groups. Similar effects have been observed for other transition metal complexes containing succinimide ligands.[12] Single crystals of **2** suitable for X-ray analysis were grown from dichloromethane/diethyl ether (1:5, v/v, ~0.1 M solution) by slow vapour diffusion (Fig. 2 Scheme 2).[17]

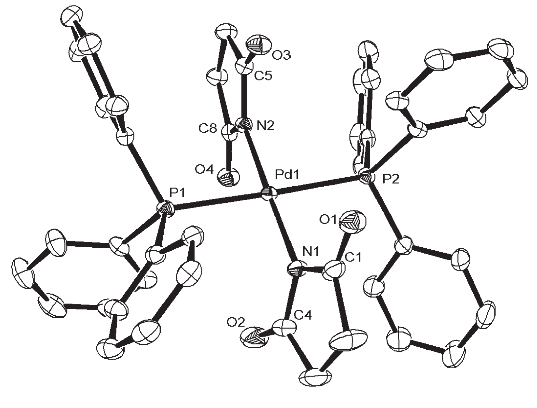
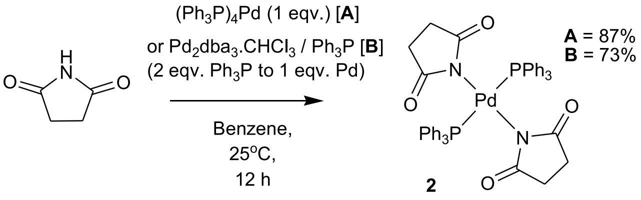


Figure 2. ORTEP representation of complex **2** with atomic labeling. Thermal ellipsoids are drawn at 50% probability. Selected bond lengths (Å): N(1)–Pd(1) 2.0364(15), N(2)–Pd(1) 2.0112(14), P(1)–Pd(1) 2.3476(5), P(2)–Pd(1) 2.3342(5); Selected bond angles: N(2)–Pd(1)–N(1) 178.34(6), N(2)–Pd(1)–P(2) 88.64(4), N(1)–Pd(1)–P(2) 90.28(5), N(2)–Pd(1)–P(1) 89.33(4), N(1)–Pd(1)–P(1) 91.75(5), P(2)–Pd(1)–P(1) 177.969(16).



Scheme 2. Synthesis of precatalyst **2**.

The X-ray crystallographic data confirms the *trans*-geometry around the Pd-centre. Interestingly, the carbonyl groups π-stack with alternatively positioned aromatic groups (Fig. 3) and the succinimide ligands deviate slightly from the plane, minimizing interactions with the nitrogen lone pair electrons (dihedral angle: C5–N2–N1–C1, θ=13°).

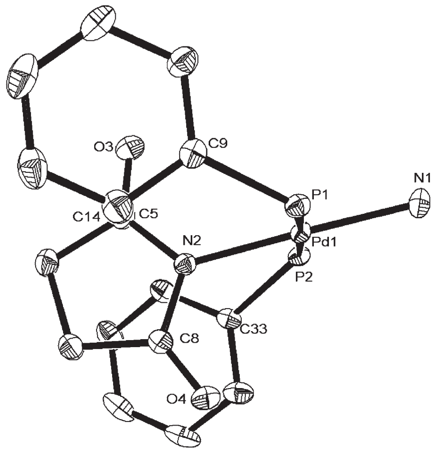
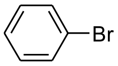
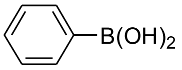
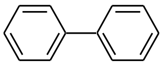
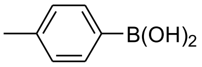
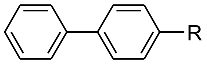
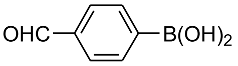
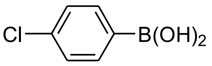
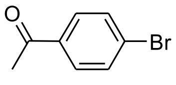
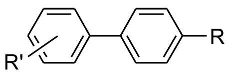
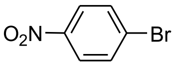
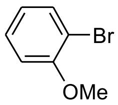
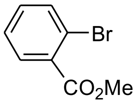
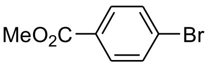
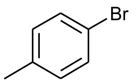
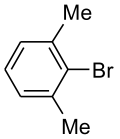
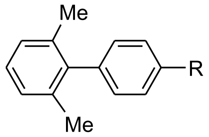


Figure 3. Selected atoms in complex **2** showing the key π-stacking interactions between the carbonyl groups and the overlapping phosphorus aromatic groups.

The positioning of the substituents around the palladium centre is a consequence of intramolecular π-stacking interactions and not intermolecular interactions between molecules within the unit cell, which is negligible. The IR spectrum of a CH_2Cl_2 solution of **2** interestingly shows two absorptions at 1723 (w) and 1645 cm^{-1} (s). The lower v(CO) frequency is attributable to the imidato-carbonyl, where Pd→σ-donation and π–π repulsions in the Pd–N bond promote delocalisation of the nitrogen lone pair on to the carbonyl group.[12] The higher stretching frequency mode at 1723 cm^{-1} is attributable to v_{sym}(CO). This band has negligible intensity compared with the antisymmetric v(CO) absorption. This data is consistent with previously reported Pd-complexes possessing succinimide ligands.[18]

Table 1. Suzuki cross-coupling of aryl halides and aryl boronic acids catalysed by (Ph$_3$P)$_2$Pd(*N*-Succ)$_2$ **2**[a]

Entry	Aryl bromide	Aryl boronic acid	Product	Time/h	Yield/%[b]
1	 **3a**	 **4a**	 **5a**	8	94; **67**
2	**3a**	 **4b**	 R=Me, **5b**	8	87; **84**
3	**3a**	 **4c**	R=CHO, **5c**	8	93; **63**
4	**3a**	 **4d**	R=Cl, **5d**	8	83; **71**
5	 **3c**	**4a**	 R′=4-COCH$_3$, R=H, **5e**	3	85; **64**
6	**3c**	**4b**	R′=4-COCH$_3$, R=Me, **5f**	3	81; **71**
7	**3c**	**4c**	R′=4-COCH$_3$, R=CHO, **5g**	3	89; **74**
8	**3c**	**4d**	R′=4-COCH$_3$, R=Cl, **5h**	3	83; **73**
9	 **3d**	**4a**	R′=4-NO$_2$, R=H, **5i**	4	95; **74**
10	**3d**	**4b**	R′=4-NO$_2$, R=Me, **5j**	5	96; **69**
11	**3d**	**4c**	R′=4-NO$_2$, R=CHO, **5k**	5	96; **74**
12	**3d**	**4d**	R′=4-NO$_2$, R=Cl, **5l**	5	89; **71**
13	 **3e**	**4a**	R′=2-OMe, R=H, **5m**	10	86; **72**
14	 **3f**	**4a**	R′=2-CO$_2$Me, R=H, **5n**	10	94; **55**
15	**3f**	**4c**	R′=2-CO$_2$Me, R=CHO, **5o**	10	**66**
16	**3f**	**4d**	R′=2-CO$_2$Me, R=Cl, **5p**	14	**56**
17	**3f**	**4a**	R′=2-CO$_2$Me, R=Me, **5q**	10	**62**
18	 **3g**	**4a**	R′=4-CO$_2$Me, R=H, **5r**	8	**74**
19	**3g**	**4c**	R′=4-CO$_2$Me, R=CHO, **5s**	8	**58**
20	 **3h**	**4a**	R′=4-Me, R=H, **5b**	8	**70**
21	 **3i**	**4a**	 R=H, **5t**	14	79; **65**
22	**3i**	**4b**	R=Me, **5u**	14	84; **59**
23	**3i**	**4c**	R=CHO, **5v**	14	70; **52**
24	**3i**	**4d**	R=Cl, **5w**	14	91; **76**

[a] *Reaction conditions*: aryl bromide (1.05 equiv., 0.45 mmol), aryl boronic acid (1.0 equiv., 0.41 mmol), **2** (1 mol%), 1 M aq. Na$_2$CO$_3$ (1 mL), THF (1.5 mL), 60 °C.

[b] Conversion by ^{1}H NMR spectroscopy. Numbers in bold are isolated yields after chromatography.

1. Suzuki cross-coupling using $(Ph_3P)_2Pd(\textit{N}\text{-}Succ)_2$ (2)

The Suzuki cross-coupling of activated and deactivated aryl bromides (**3a-i**) with four aryl boronic acids (**4a-d**) were carried out in the presence of 1 mol% of precatalyst **2** to give the cross-coupled products (**5a-w**, Table 1). Bromobenzene **3a** reacted with phenylboronic acid **4a** in 8 h to give biphenyl **5a** in 67% isolated yield (94% conversion by ^{1}H NMR spectroscopy, entry 1). The more reactive 4-methylphenylboronic acid **4b** reacted with **3a** to give the cross-coupled product **5b** in 84% isolated yield (entry 2). Both 4-formylphenylboronic acid **4c** and 4-chlorophenylboronic acid **4d** reacted with **3a** to give **5c** and **5d**, respectively in good yields (entries 3 and 4). The activated 4-acetylbromobenzene **3c** reacted with **4a-d** in 3 h and gave good isolated yields (64–73%) of the corresponding cross-coupled products (**5e-h**, entries 5–8). Similarly, 4-nitrobromobenzene **3d** gave the cross-coupled products **5i-l** in good yield (entries 9–12). In all of these reactions percentage conversion to products was generally excellent (as adjudged by ^{1}H NMR spectra of the crude reaction mixtures). The deactivated substrate, 2-bromoanisole **3e** reacted with **4a** to give **5m** in 72% isolated yield (entry 13). The more activated, but more sterically congested ester substrate **3f**, reacted with **4a**, **4c-d** to give the cross-coupled products in generally good isolated yields (entries 14–16). The less sterically demanding ester substrate **3g** reacted similarly with **4a** and **4c** to give the cross-coupled products **5r** and **5s** in 74% and 58% yields, respectively (entries 18 and 19). The deactivated substrate, 4-bromotoluene **3h**, reacted with **4a** to give the cross-coupled product **5b** in 70% isolated yield in only 8 h (entry 20). The very sterically congested and deactivated substrate, 2,6-dimethylbromobenzene **3i** did react with **4a-d** to give the cross-coupled products **5t-w** in modest to good yields, but as might be expected, the reactions took substantially longer (entries 21–24). In these examples, the percentage conversion to products was generally good.

The kinetic profile for the reaction of 4-nitrobromobenzene **3d** with phenylboronic acid **4a** in the presence of 1 mol% of **2** to give **5i** was determined at 60 °C by GC analysis (Fig. 4).[19] This shows a slight induction period, which is expected for the generation of an active catalyst species.

On analysis of the reaction mixture after ca. 10 s, we see immediate loss of Ph_3P (1 equiv. with respect to **2**). At this point, the homo- or cross-coupled products were not detected. After 0.25 h, biphenyl, the homo-coupled product, was detected (0.01 equiv. overall). The reaction then enters into a linear regime, slowly decaying after 2.3 h (~83% conversion). The formation of biphenyl after 0.33 h indicates that phenylboronic acid **4a** is involved in conversion of the Pd(II) precatalyst **2** to a Pd(0) species. Exactly 2 equiv. of **4a** (0.02 equiv.) are required for this process. It should be noted that the total concentration of biphenyl does not increase throughout the course of the reaction. For comparison, the same reaction was run in the presence of $(Ph_3P)_2PdCl_2$ (1 mol%) under identical conditions (and concentration). The reaction was slightly slower and it failed to reach completion (~12% starting material was detected). The conversion of the Pd(II) precatalyst to a Pd(0) species can be quantified similarly to precatalyst **2**. Unlike **2**, rapid loss of Ph_3P was not seen immediately. In terms of catalyst activity, **2** is similar to $(Ph_3P)_2PdCl_2$. The major advantage of **2**, for this substrate (**3d**) in particular, is that the reaction proceeded to completion under these conditions.

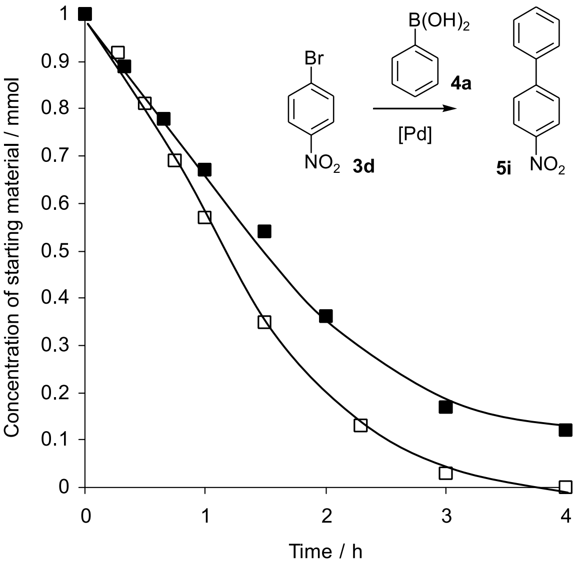


Figure 4. □ Reaction profile for the Suzuki cross-coupling reaction of 4-nitrobromobenzene **3d** (0.45 mmol) and phenylboronic acid **4a** (0.41 mmol) in THF/1 M aq. Na_2CO_3 (1.5 mL:1 mL) using precatalyst **2** (1 mol%) by GC analysis. ■ Identical reaction in the presence of $(Ph_3P)_2PdCl_2$ (1 mol%).

To assess whether **2** compares well against an alternative, but more deactivated substrate, a similar GC analysis of the reaction of 2-bromoanisole **3e** with phenylboronic acid **4a** to give **5m** under identical conditions was conducted (Fig. 5).

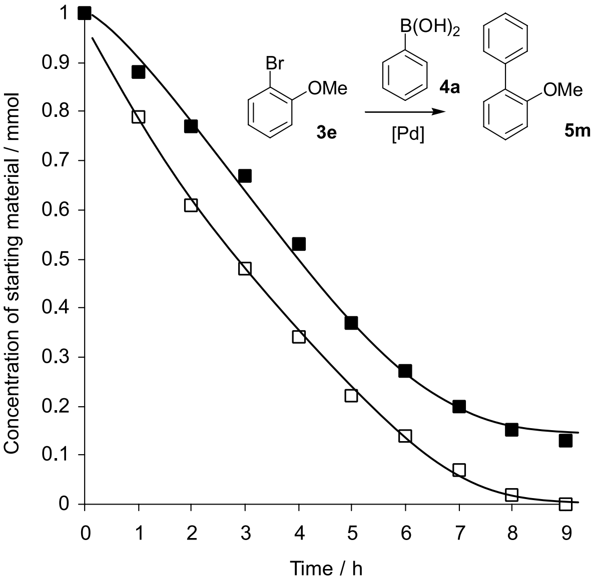


Figure 5. □ Reaction profile for the Suzuki cross-coupling reaction of 2-bromoanisole **3e** (0.45 mmol) and phenylboronic acid **4a** (0.41 mmol) in THF/1 M aq. Na_2CO_3 (1.5 mL:1 mL) using **2** (1 mol%) at 60 °C by GC analysis. ■ Identical reaction in the presence of $(Ph_3P)_2PdCl_2$ (1 mol%).

As with the reaction of **3d**, we see the rapid loss of Ph_3P (1 equiv. with respect to **2**). Biphenyl (0.01 equiv. overall) was detected at 1 h, the concentration staying constant throughout remaining course of the reaction. An induction period for **2** was less obvious in this experiment. A small induction period is seen for the $(Ph_3P)_2PdCl_2$ precatalyst. The reaction follows a similar linear regime for $(Ph_3P)_2$-$PdCl_2$, however the reaction again fails to reach completion. Indeed, we have determined that it is necessary to use 2.5 mol% of $(Ph_3P)_2PdCl_2$ for complete consumption of starting material under the conditions used.

The effect of catalyst loading on the reaction of 4-nitrobromobenzene **3d** and phenylboronic acid **4a** was compared at 2.5, 1 and 0.25 mol% **2** (Fig. 6). The reaction is noticeably faster at 2.5 mol% **2**. However, the initial rapid consumption of **3d** (50%) is followed by noticeable deceleration during the latter stages (>2 h). After this time, at 1 mol% catalyst loading, a similar quantity of **3d** has been consumed (86% at 2.5 mol% and 87% at 1 mol%). The precipitation of palladium black at the higher catalyst loading could account for this. The initial loss of Ph_3P (detected) from precatalyst **2** suggests the initial formation of a mono-ligated phosphine T-shaped palladium(II) species **V** (Scheme 3). Based on the stabilizing properties of the succinimide (vide supra) this would be expected to be in equilibrium with a dimeric species **VI**. Conversion of either the monomeric or dimeric species with **4a** would then initially generate the homo-coupled product, biphenyl, and a mono-ligated phosphine species 'Ph_3P–Pd(0)', which presumably picks up the second free phosphine to generate a more reactive bis-ligated phosphine species '$(Ph_3P)_2$Pd(0)'.[20]

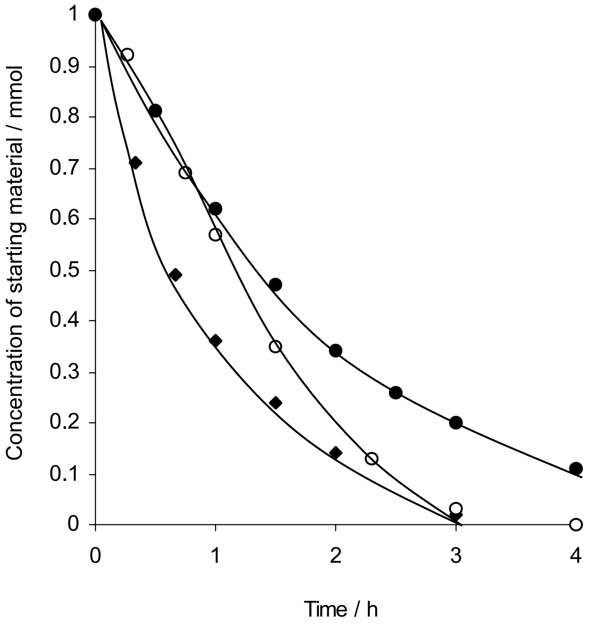
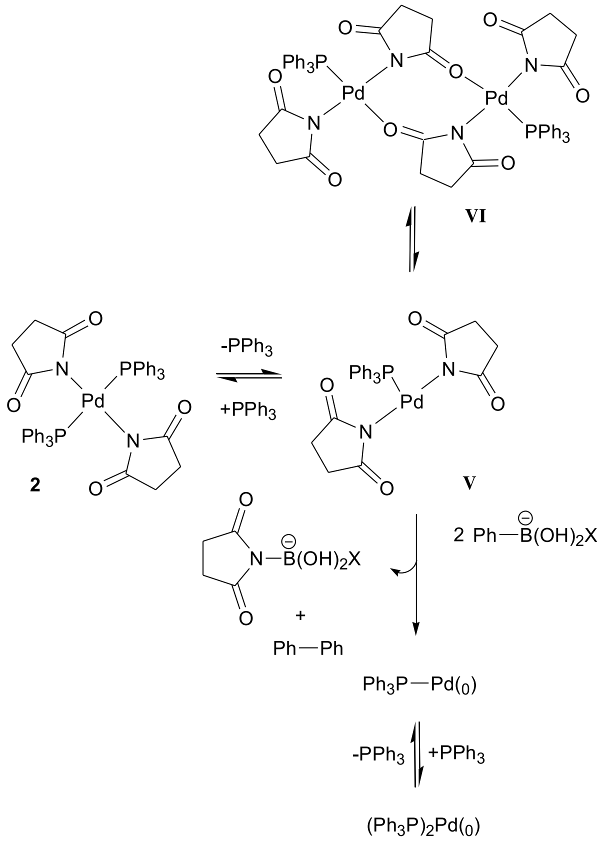


Figure 6. Reaction profile for the Suzuki cross-coupling reaction of 4-nitrobromobenzene **3d** (0.45 mmol) and phenylboronic acid **4a** (0.41 mmol) in THF/1 M aq. Na_2CO_3 (1.5 mL:1 mL) using **2** at different catalyst loadings by GC analysis: ◆ 2.5 mol% [Pd]; ○ 1.0 mol% [Pd] ● 0.25 mol% [Pd].



Scheme 3. Dissociation of Ph_3P and generation of the palladium(0) species.

However, we are able to detect the presence of free phosphine throughout the course of the reaction (by GC). To gain further details of the reactive intermediates, which lead to the generation of the active catalytic palladium species, the reaction of **3d** and **4a** was followed by ^1H and ^{31}P NMR spectroscopy using 2.5 mol% **2** at 60 °C in d_8-THF/1 M Na_2CO_3 in D_2O (1.5/1, v/v) (Fig. 7).[21]

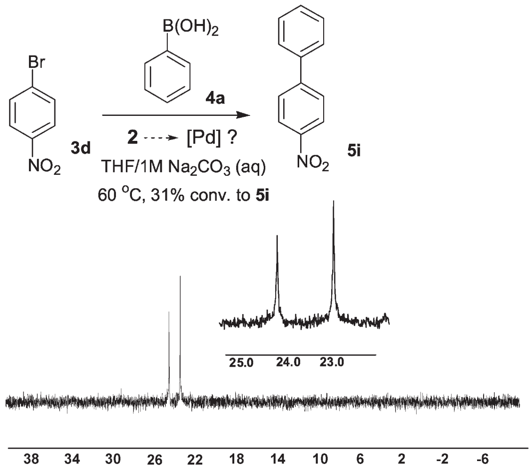
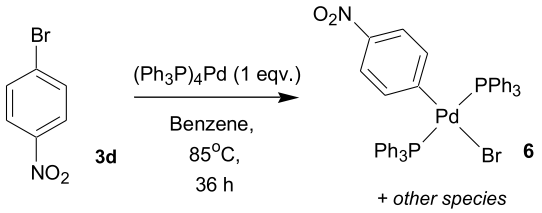


Figure 7. A snapshot of the reaction of **3d** with **4a** to give **5i** catalysed by precatalyst **2** (by ^{31}P NMR spectroscopy, 162 MHz).

The ^1H NMR spectrum (400 MHz) of the reaction mixture after ca. 1.5 h showed the presence of the cross-coupled product **5i** (31% conversion) based on consumption of **3d**. The ^{31}P NMR spectrum (162 MHz) exhibited two phosphorus signals (δ 23.09 and 24.19, integration ratio ~1.1:1) with no observable phosphorus spin–spin coupling. The signal at higher field appears to be attributable to precatalyst **2**, whereas the signal at lower field belongs to a new species. An obvious species that might be observed is the oxidative addition intermediate of $(Ph_3P)_2Pd(0)$ and **3d**. We attempted to synthesise this complex independently from $(Ph_3P)_4Pd$ (1 equiv.) and **3d** (2 equiv.) in benzene at 85 °C for 36 h (Scheme 4). The solution goes from an orange to a yellow colour during the course of the reaction. On cooling to room temperature, a dark yellow solid precipitated out of solution, which was filtered and washed with ether (56% yield). The IR spectrum of this material in CH_2Cl_2 indicates the presence of a conjugated nitro group at 1520(s) and 1358(s) cm^{-1}, due to asymmetrical and symmetrical stretching of the NO bonds. However, the ^{31}P NMR spectrum run in d_8-THF shows four signals (δ 24.19, 23.88, 23.80 and 22.80, in a ratio of approximately 1:1:4:4). We would expect to observe $^2J_{PP}$ spin–spin coupling for the *cis*-form of **6** (the initial oxidative addition intermediate), however we do not.[22]



Scheme 4. Attempted synthesis of $(Ph_3P)_2Pd(Br)$-*p*-$C_6H_4NO_2$ **6**.

The ^{31}P NMR spectrum of the same material run using $CDCl_3$ as the solvent again showed the presence of four phosphorus signals (δ 24.21, 23.89, 23.68 and 22.63), but the ratio of these were approximately 1:3.2:8.5:4.9. This suggested to us that these species are in dynamic equilibrium. Presumably this explains why this complex has not been synthesised or characterised independently.[23] At the present time we cannot confirm whether the phosphorus containing species observed at δ 24.19 is **6** or a related Pd species. The fact that a signal attributable to the precatalyst **2** is seen at δ 23.09 is intriguing in itself, as the GC analysis of the same reaction (at 1 mol% catalyst loading) indicated that all the precatalyst had been converted from Pd(II) to Pd(0)—1 equiv. of homo-coupled product was observed in the initial stages of the reaction (vide supra).[24] This suggests that either succinimido or succinimide ligand could react to regenerate the Pd(II) bis(succinimide) complex **2**. Further studies with the ^{15}N labelled succinimide complex of **2** are being carried to study this in more detail.

In summary, we have identified **2** as an active palladium(II) precatalyst for the Suzuki cross-coupling reaction. These studies have shown that there is a subtle difference between the pseudohalide ligand—succinimide and the chloride ligand, and that although it is often assumed that Pd(II) precatalysts are converted into Pd(0) species, clearly the halide/pseudohalide has an effect on the 'real' catalytically active Pd intermediates. The true involvement of the succinimide ligand, whether as an anionic ligand or activator for the arylboronic acid, is part of ongoing mechanistic studies in our laboratories.

2. Experimental

2.1. General

THF was dried over sodium–benzophenone ketyl (distilled prior to use). All reactions were conducted under an inert atmosphere of Ar or N_2 on a Schlenk line. $Pd(PPh_3)_4$ was prepared by reduction of $(Ph_3P)_2PdCl_2$ with hydrazine.[25] $(PPh_3)_2PdCl_2$ was prepared from $PdCl_2$ in refluxing DMSO and PPh_3 (2 equiv.) using a known procedure.[26] Melting points were recorded on an electrothermal IA9000 Digital Melting Point Apparatus and are uncorrected. TLC analysis was performed on Merck 5554 aluminum backed silica gel plates and compounds visualized by ultraviolet light (254 nm), phosphomolybdic acid solution (5% in EtOH), or 1% ninhydrin in EtOH. ^1H NMR spectra were recorded at 270 MHz using a JEOL EX270 spectrometer or at 400 MHz using a JEOL ECX400 spectrometer; ^{13}C NMR spectra at 67.9 or 100.5 MHz. Chemical shifts are reported ins parts per million (δ) downfield from an internal tetramethylsilane reference. Coupling constants (*J* values) are reported in hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), q (quartet), qn (quintet), sx (sextet), m (multiplet), br (broad).

GC conditions: Analysis was performed using a Varian CP-3800 GC equipped with a CP-8400 Autosampler. Separation was achieved using a DB-1 column (30 m×0.32 mm, 0.25 μm film thickness) with carrier gas flow rate of 3 ml min^{-1} and a temperature ramp from 50 to 250 °C at 20 °C min^{-1}. The injection volume was 1 μL with a split ratio of 50.

The following compounds were characterized by ^1H, ^{13}C NMR spectroscopy and mass spectrometry and compared to the known literature data: biphenyl **5a**,[27] 4-methylbiphenyl **5b**,[27] 4′-formylbiphenyl **5c**,[28] 4-chlorobiphenyl **5d**,[28] 4-acetylbiphenyl **5e**,[29] 4-acetyl-4′-methylbiphenyl **5f**,[30] 4-acetyl-4′-formylbiphenyl **5g**,[31] 4-acetyl-4′-chlorobiphenyl **5h**,[32] 4-nitrobiphenyl **5i**,[33] 4-nitro-4′-methylbiphenyl **5j**,[34] 4′-nitro-biphenyl-4-carbaldehyde **5k**,[35] 4-nitro-4′-chlorobiphenyl **5l**,[36] 2-methoxybiphenyl **5m**,[37] 2-methoxycarbonylbiphenyl **5n**,[38] 2-methoxycarbonyl-4′-formylbiphenyl **5o**,[39] 2-methoxycarbonyl-4′-chlorobiphenyl **5p**,[36] 2-methoxycarbonyl-4′-methylbiphenyl **5q**,[40] 4-methoxycarbonylbiphenyl **5r**,[38] 2-methoxycarbonyl-4′-formylbiphenyl **5s**,[39] 2,6-dimethylbiphenyl **5t**,[41] 2,6-dimethyl-4′-methylbiphenyl **5u**[29] and 2,6-dimethyl-4′-chlorobiphenyl **5w**.[42]

2.1.1. 2,6-Dimethyl-4′-formylbiphenyl (5v).

^1H NMR (400 MHz, $CDCl_3$) 9.99 (1H, s, CHO), 7.39 (2H, d, $^3J_{HH}$=6.7 Hz, 2×CH), 7.34 (1H, d, $^3J_{HH}$=6.7 Hz, CH), 7.31 (2H, m, 2×CH), 7.28 (2H, m, 2×CH), 2.37 (6H, s, $2\times CH_3$); ^{13}C NMR (400 MHz, $CDCl_3$) 192.10, 141.50, 138.34, 135.69, 134.28, 131.7, 129.95, 129.89, 126.55 and 23.84; MS (EI) *m*/*z* 210 (67, M+), 152 (54), 91 (85), 76 (26).

2.1.2. Synthesis of $(Ph_3P)_2Pd(N\text{-}Succ)_2$ (2).

Freshly prepared $(Ph_3P)_4Pd$ (170 mg, 0.147 mmol) was dissolved in dry benzene (10 cm^3) and succinimide (29.9 mg, 0.294 mmol) was added. The solution goes from an intense yellow colour to a pale yellow after only a few minutes, and a white crystalline salt begins to slowly appear. After ~12 h the solid was filtered (no special precautions), washed with benzene and dried in vacuo to give the complex as a white powder. A small quantity of the complex was crystallised from CH_2Cl_2/ether (1/5, v/v) to give colourless crystals. Yield: 100.3 mg, 82.6%. Mp=246–247 °C; MS (FAB) (*m*/*z*): 827 [(M+1), 4%], 728 [(M−*N*-Succ), 32%], 629 [(($Ph_3P)_2$Pd-1), 17%]; IR (CH_2Cl_2, cm^{-1}) 1723 and 1645; ^{1}H NMR (400 MHz, $CDCl_3$) 7.79 (12H, m), 7.34 (18H, m), 1.40 (4H, s, 2×CH_2); ^{31}P NMR (162 MHz, $CDCl_3$) 20.42.

2.1.3. Typical Suzuki reaction. Phenylboronic acid (50 mg, 0.41 mmol), bromobenzene (70.7 mg, 0.45 mmol, 1.1 equiv.), Na_2CO_3 (1 M (aq.), 1 ml), THF (1.5 mL) and catalyst **1** (3.3 mg, 4.1 μmol, 1 mol%) were degassed via three 'freeze-pump-thaw' cycles. The resulting mixture was heated at 60 °C for the specified time. The reaction mixture was allowed to cool to room temperature and water (10 mL) added. The mixture was extracted with CH_2Cl_2 (3×10 mL) and the organic extracts dried ($MgSO_4$), filtered and concentrated in vacuo. Purification by flash chromatography gave biphenyl as a white solid (42.3 mg, 67%).

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19. Response factors for GC analysis: 4-nitrobromobenzene, 1.00; 4-nitrobiphenyl, 1.40; triphenylphosphine, 2.30: GC-MS analysis of selected quenched samples was performed to ascertain the identity of the components from the reaction mixture. Linear correlations were seen for three separate concentrations of each component. In the absence of the palladium precatalyst **2**, no reaction is observed under the conditions used.
20. It is not possible to rule out the formation of higher order polynuclear palladium species, whether they be palladium clusters or colloids, which could be responsible for the catalytic reaction. It should be noted that the formation of bis-ligated palladium(0) species is not a prerequsite for the Suzuki reaction—indeed mono-ligated palladium(0) is able to catalyse the Suzuki reaction more effectively (higher turnover frequencies) which is presumably associated with promoting the rate determining transmetallation step, see: Beeby, B.; Bettington, S.; Fairlamb, I. J. S.; Goeta, A. E.; Kapdi, A. R.; Niemelä, E. H.; Thompson, A. L. *New J. Chem.* **2004**, *28*, 600–605.
21. The higher catalyst loading was used to facilitate detection of the phosphorus containing species.
22. We have been unable to purify adduct **6** by regular silica-gel column chromatography from this mixture.
23. To the best of our knowledge this complex has not been synthesised independently. Given the fact that 4-nitro-phenyl bromide is often used as a benchmark substrate in Pd-catalysed cross-coupling reactions, this is surprising. All common databases, including the Cambridge Crystallographic Database, were searched for details of this complex.
24. We have not isolated any palladium complexes (in a zero or +two oxidation state) from silica-gel chromatography. No yellow bands, which could be indicative of a palladium(II) species, were also not seen.
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