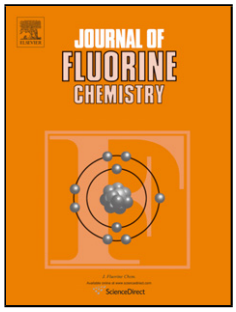

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Synthesis and reactivity of a cationic palladium complex as possible intermediate in a Suzuki-Miyaura cross-coupling reaction

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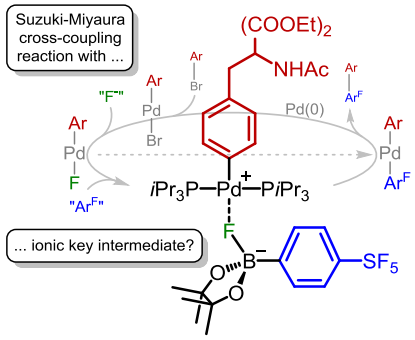
Dedicated to Prof. Antonio Togni the winner of the ACS Prize in Fluorine Chemistry 2017

Graphical Abstract



Highlights

- A fluorinated 4-aryl phenylalanine derivate containing an SF5 group was prepared as cross-coupling product.
- The high reactivity of an intermediary Pd-F complex towards a boronic ester is demonstrated.
- A cationic palladium species is obtained as conceivable intermediate in the transmetallation step.

Abstract

A stoichiometric reaction of a palladium fluorido complex with an aromatic boronic ester yielded a fluorinated 4-aryl phenylalanine derivate (aryl = 4-$C_6H_4SF_5$) as Suzuki-Miyaura cross-coupling product. Due to the high reactivity of the metal complex, the reaction proceeded smoothly at ambient temperature. Low-temperature NMR investigations revealed a possible role of *trans*-[Pd{BF(4-$C_6H_4SF_5$)(pin)}(Phe^{Et})($PiPr_3$)$_2$] (**5**, Phe^{Et} = bound phenylalanine derivative = 4-$C_6H_4CH_2C${$NHC(O)CH_3$}(CO_2Et)$_2$, pin = pinacolato = $O_2C_2Me_4$) as a potential intermediate of the transmetallation step. Compound **5** resulted from fluoride transfer from palladium to boron. The similar complex *trans*-[Pd(BF_4)(Phe^{Et})($PiPr_3$)$_2$] (**7**) was generated on treatment of the fluorido complex with $NaBF_4$. Complex **7** is not stable at room temperature. Degradation gave the phosphonium salt [$PiPr_3Phe^{Et}$][BF_4] (**4**). Interestingly, the same compound was also found in the initially mentioned cross-coupling reaction as minor product.

Keywords

palladium; boron; cross-coupling; fluorido complexes

1. Introduction

The formation of a biaryl palladium(II) complex as intermediate in the Suzuki-Miyaura cross-coupling reaction is facilitated by a base, but its role in the transmetallation step is still a matter of discussion [1]. Two distinct reaction pathways are often assumed to be decisive for conversion of an oxidative addition product at a metal center with a

boronic acid or ester in the presence of a base [1e, 1f, 1l]. On the one hand the base could react with the boronic compound to generate a more nucleophilic boronate first, capable of reacting with the oxidative addition product. On the other hand, the base might replace the metal-bound halogen atom of the oxidative addition product. The resulting complex can be of higher reactivity towards the boronic acid or ester. Both possibilities might facilitate a proper transmetallation which yields a biaryl palladium(II) compound. Amatore, Jutand and coworkers described antagonistic effects using fluoride or hydroxide as base in the coupling [1h, 1i, 1k-n]. They revealed that the fluorido complex *trans*-[PdF(4-C_6H_4CN)(PPh_3)$_2$] is a highly reactive key intermediate in the transmetallation step whereas the boronates [$B(C_6H_5)(OH)_{3-n}(F)_n$]$^-$ (n = 1-3) have to be regarded as unreactive compounds [1h, 1i]. Thus, a transmetallation via a fluorido complex is clearly favored. It has been reported that the fluorido complex *trans*-[PdF(Phe^{Et})($P\textit{i}Pr_3$)$_2$] (**1**) revealed a remarkable high reactivity towards the boronic ester 2-BpinC_5NF_4 [1a]. Note that **1** was synthesized by treatment of its bromo analogue *trans*-[PdBr(Phe^{Et})($P\textit{i}Pr_3$)$_2$], with NMe_4F in CD_2Cl_2 at room temperature [1a]. However, the complex *trans*-[Pd{BF(2-C_5NF_4)(pin)}(Phe^{Et})($P\textit{i}Pr_3$)$_2$] was observed after a fluoride transfer from palladium to boron and is assumed to be an intermediate or a resting state of the coupling reaction [1e, 1f, 1m, 1n, 2]. In this contribution, we report on the reactivity of the fluorido complex *trans*-[PdF(Phe^{Et})($P\textit{i}Pr_3$)$_2$] (**1**) towards the boronic ester 4-Bpin$C_6H_4SF_5$ and also of **1** with $NaBF_4$.

2. Results and discussion

Treatment of the fluorido complex *trans*-[PdF(Phe^{Et})($P\textit{i}Pr_3$)$_2$] (**1**) with equimolar amounts of the boronic ester 4-Bpin$C_6H_4SF_5$ in the absence of additional base at room temperature led to the formation of the cross-coupling product (4-$C_6H_4SF_5$)Phe^{Et} (**2**) as major product within 2 hours (Scheme 1). Additionally, [Pd($P\textit{i}Pr_3$)$_2$] (**3**), FBpin and minor amounts of the phosphonium salt [4-$P\textit{i}Pr_3Phe^{Et}$][BF_4] (**4**) were formed. The reaction includes a transmetallation and a reductive elimination step, which are considered to be key-steps of Suzuki-Miyaura cross-coupling reactions. **2** and **4** were characterized by their NMR spectroscopic and HR ESI/MS data. Analytical data for [Pd($P\textit{i}Pr_3$)$_2$] (**3**) are in accordance to literature data [1a, 3]. FBpin was identified by its $^{11}B\{^1H\}$ NMR spectrum, where its signal appears as a broad singlet at δ = 22 ppm [4].

The reaction of **1** with 4-Bpin$C_6H_4SF_5$ was monitored by variable-temperature NMR spectroscopy starting from -80 °C in [D_8]THF. The $^{19}F\{^1H\}$, $^{31}P\{^1H\}$ and $^{11}B\{^1H\}$ NMR studies revealed the formation of the compound *trans*-[Pd{BF(4-$C_6H_4SF_5$)(pin)}(Phe^{Et})($P\textit{i}Pr_3$)$_2$] (**5**) between -80 °C to 10 °C (Scheme 2, Figure 1 and 2). Compound **5** resulted from a fluoride transfer from the palladium atom of **1** to the boron atom of 4-Bpin$C_6H_4SF_5$. Note that ionic intermediates in cross-coupling reactions were considered before [1a, 1e-f, 2b, 2c, 2e, 2f, 2h, 2j]. Although we have no distinct experimental evidence, it is rather likely that the cation *trans*-[Pd(Phe^{Et})($P\textit{i}Pr_3$)$_2$]$^+$ and its anionic boronate interact with each other like it is the case for [Pd(BF_4)(CF=CFCF_3)(PCy_3)$_2$] [5]. Alternatively, the free coordination side at Pd could also be vacant or coordinated by [D_8]THF. The possibility that the transmetallation product *trans*-[Pd(Phe^{Et})(4-$C_6H_4SF_5$)($P\textit{i}Pr_3$)$_2$] instead of **5** is formed can be ruled out since no signal for FBpin, which should be liberated simultaneously, was observed by $^{11}B\{^1H\}$ NMR spectroscopy as it was the case for the room temperature attempt described above. For the cation of **5**, a singlet at δ = 30.9 ppm was obtained by $^{31}P\{^1H\}$ NMR spectroscopy at -50 °C. No coupling to fluorine was detected, as it is the case in the starting compound **1**. For the boronate [BF(4-$C_6H_4SF_5$)(pin)]$^-$, three resonances at δ = 88.7, 63.6 and -128.5 ppm were found by $^{19}F\{^1H\}$ NMR spectroscopy at the same temperature. The first two signals, a quintet and a doublet, were assigned to the SF_5 group of **5**, each with a $^2J_{F,F}$ coupling constant of 149 Hz [6]. The latter signal at -128.5 ppm resulted from the fluoride of the B–F unit. A broad singlet at δ = 6.1 ppm in the $^{11}B\{^1H\}$ NMR spectrum was found for the boron atom of **5** at -20 °C. The chemical shift of the signals for the anion [BF(4-$C_6H_4SF_5$)(pin)]$^-$ of **5** are in good accordance to data for [BF(4-$C_6H_4SF_5$)(pin)]$^-$ with Cs^+ as counter ion [1a].

However, the formation of *trans*-[Pd{BF(4-$C_6H_4SF_5$)(pin)}(Phe^{Et})($P\textit{i}Pr_3$)$_2$] (**5**) at low temperature was not quantitative. In fact, the fluorido complex *trans*-[PdF(Phe^{Et})($P\textit{i}Pr_3$)$_2$] (**1**) remained as main complex in between -80 to 10 °C (Scheme 2, Figures 1 and 2). While the concentration of **5** compared to **1** increased from -80 to -50 °C, a reversed tendency was found by elevating the temperature further until no signal for **5** was detected at -10 °C by $^{31}P\{^1H\}$ NMR spectroscopy (Figure 1). In between -10 to 10 °C, signals for both complexes possibly obscure each other, which impedes the detection of **5**. Note that signals for the corresponding boronate of **5** were observed up to 10 °C by $^{19}F\{^1H\}$ NMR spectroscopy (Figure 2). According to the $^{31}P\{^1H\}$ NMR spectra at various temperatures, the highest concentration of **5** was obtained at -50 °C with a ratio for **1** to **5** of 3:1. The generation of **1** seems to be thermodynamically preferred at low-temperature. On the other hand, the polarity of THF increases by lowering the temperature which might in turn favor the formation of ionic compound **5** [7]. These opposing effects might explain the simultaneous observation of **1** and **5** in different ratios at different temperatures.

Above -10 °C, the cross-coupling product (4-$C_6H_4SF_5$)Phe^{Et} (**2**) was liberated along with [Pd($P\textit{i}Pr_3$)$_2$] (**3**) and FBpin (Scheme 3, Figure 1 to 2). At room temperature, minor amounts of the bifluorido complex *trans*-[Pd(FHF)(Phe^{Et})($P\textit{i}Pr_3$)$_2$] (**6**) were identified (Scheme 3, Figures 1 and 2). Interestingly, this complex also reacted with 4-Bpin$C_6H_4SF_5$ to give the same coupling product **2**.

The transmetallation might be facilitated by a nucleophilic transfer of the aromatic moiety from boron to palladium in complex *trans*-[Pd{BF(4-$C_6H_4SF_5$)(pin)}(Phe^{Et})($P\textit{i}Pr_3$)$_2$] (**5**). The reactivity of cationic palladium complexes against boronic acids and boronates was described before [1e-f, 1m-n, 2a-d, 2f-h, 2j, 8]. Note that boronates were often found to be unreactive in Suzuki-Miyaura cross-coupling reactions towards neutral Pd complexes [1b-d, 1g-i, 1l, 1o]. However, the transmetallation may alternatively proceed by a direct reaction of *trans*-[PdF(Phe^{Et})($P\textit{i}Pr_3$)$_2$] (**1**) with 4-Bpin$C_6H_4SF_5$ without **5** as intermediate (Scheme 3). The presented experimental NMR data do not exclude one of these two

possibilities, but investigations on a reaction of *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) with 2-BpinC$_5$NF$_4$ gave quantitative amounts of complex *trans*-[Pd{BF(2-C$_5$NF$_4$)(pin)}(Phe^{Et})(P*i*Pr$_3$)$_2$] at low temperatures [1a]. By elevating the temperature, the transmetallation proceeded without any detectable reformation of *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**), which supports the possible role of cationic palladium complexes as intermediates.

However, the formation of a bifluorido complex such as **6** from a fluorido complex requires the presence of HF. If HF is liberated *in situ* it may result from a preceding reaction of *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) with adventitious water. This should additionally give a palladium hydroxido complex but no signals for such compound were identified in the NMR spectra shown in Figure 1. Moreover, it is rather unlikely that the fluorido complex *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) contained traces of water from the outset since **1** was thoroughly characterized prior to this work and no signals for a FHF complex were obtained while handling a solution of the pure complex **1** in [D$_8$]THF [1a]. Possibly, HF or water resulted from contamination of the commercially available boronic ester 4-BpinC$_6$H$_4$SF$_5$ although NMR data of a solution of the boronic compound in [D$_8$]THF at room temperature and at -60 °C did not give any experimental evidence. However,the HF of the bifluoride ligand in complex **6** can be removed by shaking the reaction mixture in the presence of CsF [9].

Treatment of the fluorido complex **1** with 4-BpinC$_6$H$_4$SF$_5$ in an independent experiment *at room temperature* also led to the *in situ* generation of *trans*-[Pd(FHF)(Phe^{Et})(P*i*Pr$_3$)$_2$] (**6**) within minutes. Cooling the reaction solution inside the NMR machine to -65 °C allowed to identify **6**. At -65 °C, the ^{19}F{^{1}H} NMR data for **6** revealed two broad doublets at δ = -181.2 (Pd–FH*F*) and -276.5 ppm (Pd–*F*HF) with a $^2J_{F,F}$ coupling constants of 116 Hz. In the same spectrum, the signal for the fluorido complex **1** appeared at -302.7 ppm as a broad singlet. Both complexes occurred in a ratio of 1:6 as determined by integration of their resonances in the ^{19}F NMR spectrum at -65 °C. In contrast, the ^{19}F{^{1}H} NMR spectrum, recorded at room temperature, gave only one broad singlet for the metal bound fluorido ligands of both complexes at δ = -300.6 ppm, possibly because of exchange of HF or a fluoride/bifluoride exchange [10]. Grushin *et al.* showed that the transfer of HF from a Pd–FHF complex to a Pd–F compound could take place in a mixture of Pd–F/FHF complexes [10a-b, 10d]. However, the resonance for Pd–FH*F* appears at δ = -183.6 ppm as a broad singlet. Without proton decoupling, a broad doublet was obtained for the same fluorine atom at a similar chemical shift with a $^1J_{H,F}$ coupling constant of 396 Hz. The same coupling constant was observed for a broad doublet at δ = 11.77 ppm in the ^{1}H{^{31}P} NMR spectrum at room temperature, and the signal can be assigned to the proton of the bifluorido unit. Pd–FHF complexes with comparable chemical shifts and coupling constants were described before and the data indicate that **6** is of the type Pd–F···HF rather than Pd···FHF [10-11]. No separate signals were obtained for **1** and **6** by (low temperature) ^{31}P{^{1}H} NMR spectroscopy.

Additionally, *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) was treated with an excess of NaBF$_4$ in [D$_8$]THF at room temperature to form a complex comparable to *trans*-[Pd{BF(4-C$_6$H$_4$SF$_5$)(pin)}(Phe^{Et})(P*i*Pr$_3$)$_2$] (**5**). After 1 h, the NMR spectroscopic data revealed the formation of *trans*-[Pd(BF$_4$)(Phe^{Et})(P*i*Pr$_3$)$_2$] (**7**) as major compound. Signals for of [Pd(P*i*Pr$_3$)$_2$] (**3**) and [P*i*Pr$_3$Phe^{Et}][BF$_4$] (**4**) in minor amounts were also found and the fluorido complex **1** was partly consumed (Scheme 4, Figure 3). Complex **7** and **1** are present in a ratio of 1.2:1.0 according to integration of their signals in the ^{1}H NMR spectrum. The ^{31}P{^{1}H} NMR spectrum showed a signal at δ = 32.4 ppm of **7** which was obscured by signal for **1**. *trans*-[Pd(BF$_4$)(Phe^{Et})(P*i*Pr$_3$)$_2$] (**7**) is not stable at room temperature. After 22 hours, the reaction mixture turned brownish and a black precipitate was formed. Most likely, this solid resulted from the formation of Pd particles. The ^{31}P{^{1}H} NMR data showed signals corresponding to [Pd(P*i*Pr$_3$)$_2$] (**3**) and [P*i*Pr$_3$Phe^{Et}][BF$_4$] (**4**) as additional decomposition products in a ratio of 1.0:3.4 (Scheme 4, Figure 2).

It is assumed that the formation of the phosphonium salt **4** resulted from decomposition of the cationic complex *trans*-[Pd(BF$_4$)(Phe^{Et})(P*i*Pr$_3$)$_2$] (**7**). Interestingly, signals for **4** are also found in catalytic and stoichiometric Suzuki-Miyaura cross-coupling reactions using *trans*-[PdBr(Phe^{Et})(P*i*Pr$_3$)$_2$] and *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) [1a], e.g. for a reaction with 4-BpinC$_6$H$_4$SF$_5$. Thus, the detection of phosphonium salts might be an indication for the participation of cationic complexes in such couplings. The observation of *trans*-[Pd{BF(4-C$_6$H$_4$SF$_5$)(pin)}(Phe^{Et})(P*i*Pr$_3$)$_2$] (**5**) or *trans*-[Pd{BF(2-C$_5$NF$_4$)(pin)}(Phe^{Et})(P*i*Pr$_3$)$_2$] [1a] as intermediates in related model reactions additionally supports this idea.

3. Conclusions

It was demonstrated that *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) is highly reactive towards the boronic compound 4-BpinC$_6$H$_4$SF$_5$. The reaction yielded the cross-coupling product (4-C$_6$H$_4$SF$_5$)Phe^{Et} (**2**). Note that compounds with SF$_5$ are of considerable importance for materials and medicine [12]. Low temperature studies reveal that the complex *trans*-[Pd{BF(4-C$_6$H$_4$SF$_5$)(pin)}(Phe^{Et})(P*i*Pr$_3$)$_2$] (**5**) is formed, which might serve as an intermediate or is a resting state in the C–C coupling reaction. In principle the [BF(4-C$_6$H$_4$SF$_5$)(pin)]$^-$ anion might transform either a fluorine or C$_6$H$_4$SF$_5$ to the palladium centre in [Pd(Phe^{Et})(P*i*Pr$_3$)$_2$]$^+$. Thus, it remains a matter of discussion whether the formation of a transmetallation product proceeds from the fluorido complex **2** by the intermediate formation of **5** or not. The generation of cationic compounds from *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) was further demonstrated by the generation of *trans*-[Pd(BF$_4$)(Phe^{Et})(P*i*Pr$_3$)$_2$] (**7**). The Complex **7** is a source of the amino acid derivative [P*i*Pr$_3$Phe^{Et}][BF$_4$] (**4**).

4. Experimental Section

4.1 General

All reactions were carried out using Schlenk techniques and a glove box under an inert gas atmosphere of Argon. *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) [1a] was synthesized in accordance to the literature. [D$_8$]THF was dried over Solvana® and distilled before use. 4-BpinC$_6$H$_4$SF$_5$ was purchased from Manchester Organics and used without further purification. All NMR data were recorded using a Bruker DPX 300, Bruker Avance II 300, Bruker Avance III 300 or Bruker Avence III 500. ^{1}H NMR chemical shifts were referenced to residual proton of [D$_7$]THF (δ = 3.58 ppm). ^{31}P{^{1}H} NMR spectra were referenced to external H$_3$PO$_4$ (δ = 0.0 ppm), ^{19}F NMR spectra to CFCl$_3$ (δ = 0.0 ppm) and ^{11}B NMR spectra to BF$_3$·OEt (δ = 0.0 ppm). If not stated otherwise, NMR spectra were recorded at room temperature. MS (ESI) data were obtained using a Thermo Fisher Scientific FT-ICR-MS or a Agilent Technologies 6210 TOF LC/MS.

4.2 Treatment of *trans*-[PdF(Phe^{Et})(PiPr$_3$)$_2$] (**1**) with 4-BpinC$_6$H$_4$SF$_5$

A: A solution of *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) (58 mg, 77 µmol) in [D$_8$]THF (0.6 mL) was added to a solution of 4-BpinC$_6$H$_4$SF$_5$ (25.4 mg, 77 µmol) in [D$_8$]THF (0.5 mL) at -40 °C. Then, the reaction was monitored for 2 h at room temperature. Within 2 h, the solutions color changes from yellowish via an intense yellow to red. The NMR spectroscopic data after 2 h revealed the quantitative formation of **1** into (4-C$_6$H$_4$SF$_5$)Phe^{Et} (**2**) and [P*i*Pr$_3$Phe^{Et}]$^+$ (**4'**) in a ratio of 8:1 (according to the ^{1}H NMR spectrum, based on integration of the signal for the acetyl group). Furthermore, [Pd(P*i*Pr$_3$)$_2$] (**3**) [1a, 3], FBpin [4] and traces of [BF$_4$]$^-$ [4] were formed. The palladium complex **3** and compound **4** were detected in a ratio of 5.5:1.0 according to integration of their signals in the ^{31}P{^{1}H} NMR spectrum. After a reaction time of 5 min, signals corresponding to *trans*-[Pd(FHF)(Phe^{Et})(P*i*Pr$_3$)$_2$] (**6**) were intermediary obtained.

B: At -80 °C, a solution of 4-BpinC$_6$H$_4$SF$_5$ (6.6 mg, 20 µmol) in [D$_8$]THF (0.3 mL) was added to a Young NMR tube, equipped with a solution of *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) (15.0 mg, 20 µmol) in [D$_8$]THF (0.3 mL). The reaction was monitored from -80 °C to room temperature. After 20 h at room temperature, the same reaction products as in **A** were obtained in comparable ratios. Intermediary, the formation of *trans*-[Pd{BF(4-C$_6$H$_4$SF$_5$)(pin)}(Phe^{Et})(P*i*Pr$_3$)$_2$] (**5**), *trans*-[Pd(FHF)(Phe^{Et})(P*i*Pr$_3$)$_2$] (**6**) and an unkown species which shows in the ^{31}P{^{1}H}-NMR a signal at δ = 28.8 ppm (s) were detected.

C: A Young NMR tube was charged with a solution of 4-BpinC$_6$H$_4$SF$_5$ (8.8 mg, 27 µmol) in [D$_8$]THF (0.2 mL). At -50 °C, a solution of *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) (20.0 mg, 27 µmol) in [D$_8$]THF (0.5 mL) was added to the Young NMR tube. The NMR spectroscopic data at room temperature revealed the formation of *trans*-[Pd(FHF)(Phe^{Et})(P*i*Pr$_3$)$_2$] (**6**). After 20 min at room temperature, the reaction solution was cooled to -65 °C inside the NMR spectrometer. At -65 °C, **6** and **1** were present in a ratio of 1:6 according to integration of their signals in the ^{19}F NMR spectrum. After the measurement, the reaction solution was transferred into a NMR tube equipped with CsF (10.0 mg, 66 µmol) at -30 °C. After suspending the mixture for 1 min at room temperature, the NMR spectroscopic data at -65 °C revealed the presence of complex **1**. No signal for **6** was detected. Analytical data for 4-(4-C$_6$H$_4$SF$_5$)C$_6$H$_4$CH$_2$C{NHC(O)CH$_3$}(CO$_2$Et)$_2$ (**2**): ^{1}H NMR (500.1 MHz, [D$_8$]THF): δ 7.89 (dm, $^3J_{H,H}$ = 9 Hz, 2H, Ar*H*), 7.77 (dm, $^3J_{H,H}$ = 9 Hz, 2H, Ar*H*), 7.59 (dm, $^3J_{H,H}$ = 8 Hz, 2H, Ar*H*), 7.34 (s, 1H, N*H*), 7.16 (dm, $^3J_{H,H}$ = 8 Hz, 2H, Ar*H*), 4.20 (m, 4H, OC*H*$_2$CH$_3$), 3.65 (s, 2H, C*H*$_2$Ar), 1.93 (s, 3H, C(O)C*H*$_3$), 1.25 (t, $^3J_{H,H}$ = 7 Hz, OCH$_2$C*H*$_3$; the latter resonance is obscured by a signal of [Pd(P*i*Pr$_3$)$_2$] (**3**)). ^{19}F{^{1}H} NMR (470.6 MHz, [D$_8$]THF): δ 84.5 (quint, $^2J_{F,F}$ = 149 Hz, 1F), 62.5 (d, $^2J_{F,F}$ = 149 Hz, 4F). HRMS (ESI): *m/z*: calcd. for C$_{22}$H$_{25}$F$_5$NO$_5$S [*M*+H]$^+$: 510.1368; found: 510.1368. Analytical data for *trans*-[Pd{BF(4-C$_6$H$_4$SF$_5$)(pin)}{4-C$_6$H$_4$CH$_2$C{NHC(O)CH$_3$}(CO$_2$Et)$_2$}(P*i*Pr$_3$)$_2$] (**5**): ^{19}F{^{1}H} NMR (282.4 MHz, [D$_8$]THF, -50 °C): δ 88.7 (quint, $^2J_{F,F}$ = 149 Hz, 1F, S*F*$_5$), 63.6 (d, $^2J_{F,F}$ = 149 Hz, 4F, S*F*$_5$), -128.5 (s, br, 1F, B*F*). ^{31}P{^{1}H} NMR (121.5 MHz, [D$_8$]THF, -50 °C): δ 30.9 (s). ^{11}B{^{1}H} NMR (96.3 MHz, [D$_8$]THF, -20 °C): δ 6 (s, br). Note that no resonances for **5** nor the remaining starting material 4-BpinC$_6$H$_4$SF$_5$, were detected by ^{11}B{^{1}H} NMR spectroscopy at -50 °C, probably due to broadening of the signals and low intensity. Analytical data for *trans*-[Pd(FHF){4-C$_6$H$_4$CH$_2$C{NHC(O)CH$_3$}(CO$_2$Et)$_2$}(P*i*Pr$_3$)$_2$] (**6**): ^{1}H{^{19}F} NMR (300.1 MHz, [D$_8$]THF): δ 11.77 (s, br, F*H*F). ^{1}H{^{19}F} NMR (300.1 MHz, [D$_8$]THF, -65 °C): δ 12.12 (m, F*H*F). ^{1}H{^{31}P} NMR (300.1 MHz, [D$_8$]THF): δ 11.77 (d, br, $^1J_{H,F}$ = 396 Hz, F*H*F). ^{1}H{^{31}P} NMR (300.1 MHz, [D$_8$]THF, -65 °C): δ 12.12 (m, F*H*F). Other resonances in the ^{1}H NMR spectra were obscured by the presence of the other complexes in solution and could therefore not be identified.^{19}F NMR (282.4 MHz, [D$_8$]THF): δ -183.6 (d, br, $^1J_{H,F}$ = 396 Hz, FH*F*), -300.6 (s, br, *F*HF). ^{19}F NMR (282.4 MHz, [D$_8$]THF, -65 °C): δ -181.2 (m, 1F, FH*F*), -276.5 (m, 1F, *F*HF). ^{19}F{^{1}H} NMR (282.4 MHz, [D$_8$]THF): δ -183.6 (s, br, FH*F*), -300.6 (s, br, *F*HF). ^{19}F{^{1}H} NMR (282.4 MHz, [D$_8$]THF, -65 °C): δ -181.2 (d, br, $^2J_{F,F}$ = 116 Hz, 1F, FH*F*), -276.5 (d, br, $^2J_{F,F}$ = 116 Hz, 1F, *F*HF). ^{31}P{^{1}H} NMR (121.5 MHz, [D$_8$]THF): δ 32.2 (m). ^{31}P{^{1}H} NMR (121.5 MHz, [D$_8$]THF, -65 °C): δ 30.9 (m).

4.3 Treatment of *trans*-[PdF(Phe^{Et})(PiPr$_3$)$_2$] (**1**) with NaBF$_4$

NaBF$_4$ (3.6 mg, 33 µmol) was suspended in a solution of **1** (10.0 mg, 14 µmol) in [D$_8$]THF (0.5 mL) and the reaction was monitored by NMR spectroscopy. Within 22 h, the colorless solution turned to yellow to brown and a black precipitate was formed. After 22 h, the fluorido complex **1** was quantiatively consumed. Signals for [Pd(P*i*Pr$_3$)$_2$] (**3**) [1a, 3] and [P*i*Pr$_3$Phe^{Et}][BF$_4$] (**4**) were detected in a ratio of 1.0:3.4 according to integration of their signals in the ^{31}P{^{1}H} NMR spectrum. Intermediary, resonances assigned for *trans*-[Pd(BF$_4$)(Phe^{Et})(P*i*Pr$_3$)$_2$] (**7**) were detected. Analytical data for [4-P*i*Pr$_3$C$_6$H$_4$CH$_2$C{NHC(O)CH$_3$}(CO$_2$Et)$_2$][BF$_4$] (**4**) (partly published before [1a]): ^{1}H NMR (300.1 MHz, [D$_8$]THF): δ 7.93 (dd, d in ^{1}H{^{31}P} NMR spectrum, $J_{P,H}$ = 10, $^3J_{H,H}$ = 8 Hz, 2H, Ar*H*), 7.59 (s, 1H, N*H*), 7.47 (dd, d in ^{1}H{^{31}P} NMR spectrum,

$^3J_{H,H}$ = 8, $J_{P,H}$ = 3 Hz, 2H, Ar*H*), 4.18 (m, 4H, OCH_2CH$_3$), 3.71 (s, 2H, CH_2Ar), 3.44 (m, sept in ^{1}H{^{31}P} NMR spectrum, $^3J_{H,H}$ = 7 Hz, 3H, P{C*H*(CH$_3$)$_2$}$_3$), 1.95 (s, 3H, (CO)CH_3), 1.38 (dd, d in ^{1}H{^{31}P} NMR spectrum, $^3J_{P,H}$ = 16, $^3J_{H,H}$ = 7 Hz, 18H; P{CH(CH_3)$_2$}$_3$), 1.22 (t, $^3J_{H,H}$ = 7 Hz, OCH$_2$CH_3, the resonance is obscured by a signal of [Pd(P*i*Pr$_3$)$_2$] (**3**)).^{19}F{^{1}H} NMR (282.4 MHz, [D$_8$]THF): *δ* -152.5 (s, BF_4^-). ^{31}P{^{1}H} NMR (121.5 MHz, [D$_8$]THF): *δ* 41.1 (s). MS (ESI), *m/z*: calcd. for $C_{25}H_{41}NO_5P$ [M]$^+$ 466.271; found: 466.276. Analytical data for *trans*-[Pd(BF$_4$){4-C$_6$H$_4$CH$_2$C{NHC(O)CH$_3$}(CO$_2$Et)$_2$}(P*i*Pr$_3$)$_2$] (**7**): ^{1}H NMR (300.1 MHz, [D$_8$]THF): *δ* 7.27 (d, $^3J_{H,H}$ = 8 Hz, Ar*H*), 6.80 (s, br, N*H*), 6.66 (d, $^3J_{H,H}$ = 8 Hz, Ar*H*), 4.16 (m, OCH_2CH$_3$), 3.45 (s, CH_2Ar), 2.18 (m, P{C*H*(CH$_3$)$_2$}$_3$), 1.91 (s, C(O)CH_3), 1.33-1.18 (m, P{CH(CH_3)$_2$}$_3$ and OCH$_2$CH_3) (all signals were obscured by signals for **1** or **4**. ^{19}F{^{1}H} NMR (282.4 MHz, [D$_8$]THF): *δ* -156.4 ppm (s, br, BF_4^-). ^{31}P{^{1}H} NMR (121.5 MHz, [D$_8$]THF): *δ* 32.4 (obscured by signal for **1**).

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Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version.

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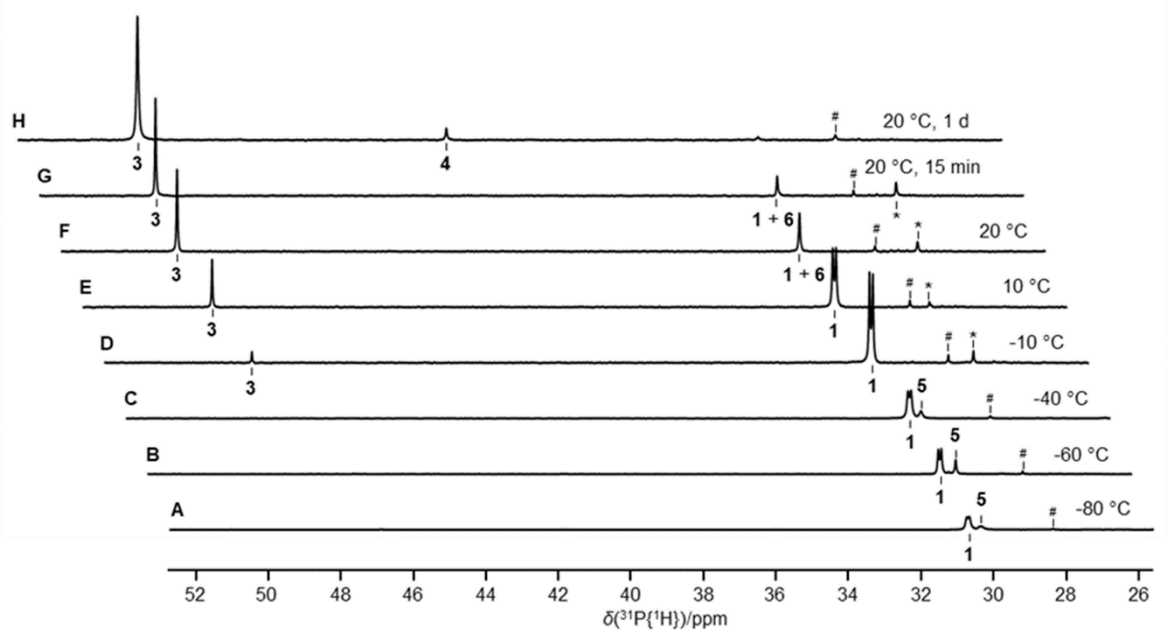


Figure 1. $^{31}P\{^{1}H\}$ NMR spectra of the treatment of *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) with 4-BpinC$_6$H$_4$SF$_5$ in [D$_8$]THF at various temperatures. **A**-**C** Fluorido complex **1** and *trans*-[Pd{BF(4-C$_6$H$_4$SF$_5$)(pin)}(Phe^{Et})(P*i*Pr$_3$)$_2$] (**5**). **D**-**G** Formation of [Pd(P*i*Pr$_3$)$_2$] (**3**) (along with the cross-coupling product (4-C$_6$H$_4$SF$_5$)Phe^{Et} (**2**), FBpin) and an unknown compound *****. **F**-**G** Formation of *trans*-[Pd(FHF)(Phe^{Et})(P*i*Pr$_3$)$_2$] (**6**) at room temperature which is at equilibirium with **1**. **H** Formation of [Pd(P*i*Pr$_3$)$_2$] (**3**) and [4-P*i*Pr$_3$Phe^{Et}][BF$_4$] (**4**) in a ratio of 5.5:1 as final phosphorus containing products. # *trans*-[PdCl(Phe^{Et})(P*i*Pr$_3$)$_2$] from the synthesis of the Pd fluorido complex **1** [1a].

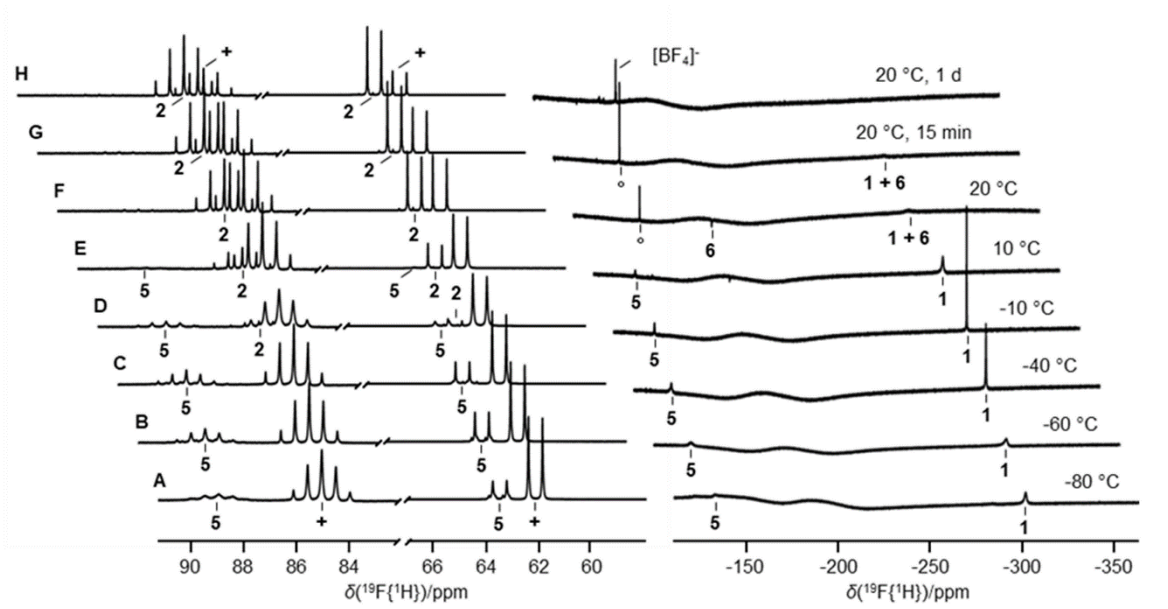


Figure 2. $^{19}F\{^{1}H\}$ NMR spectra of the reaction of *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) with 4-BpinC$_6$H$_4$SF$_5$ (**+**) in [D$_8$]THF at various temperatures. **A**-**E** Fluorido complex **1**, 4-BpinC$_6$H$_4$SF$_5$ (**+**) and *trans*-[Pd{BF(4-C$_6$H$_4$SF$_5$)(pin)}(Phe^{Et})(P*i*Pr$_3$)$_2$] (**5**). **D**-**H** Formation of the cross-coupling product (4-C$_6$H$_4$SF$_5$)Phe^{Et} (**2**) (along with [Pd(P*i*Pr$_3$)$_2$] (**3**) and FBpin). **F**-**G** Formation of *trans*-[Pd(FHF)(Phe^{Et})(P*i*Pr$_3$)$_2$] (**6**) at room temperature which is at equilibirium with **1**. **F**-**H** Unknown compound **°** and formation of [BF$_4$]$^-$ as a minor product.

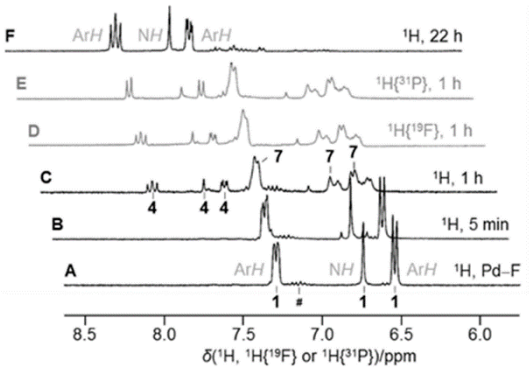
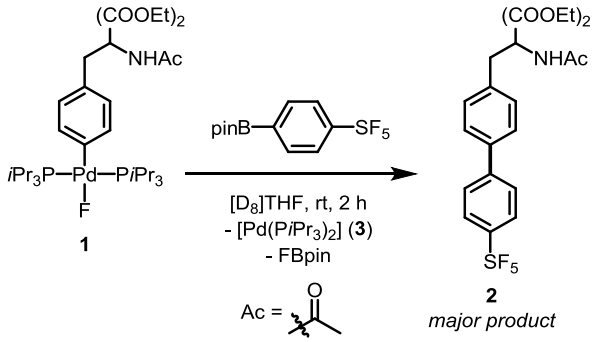
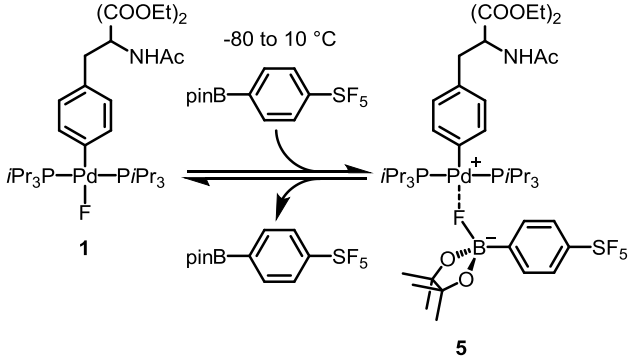


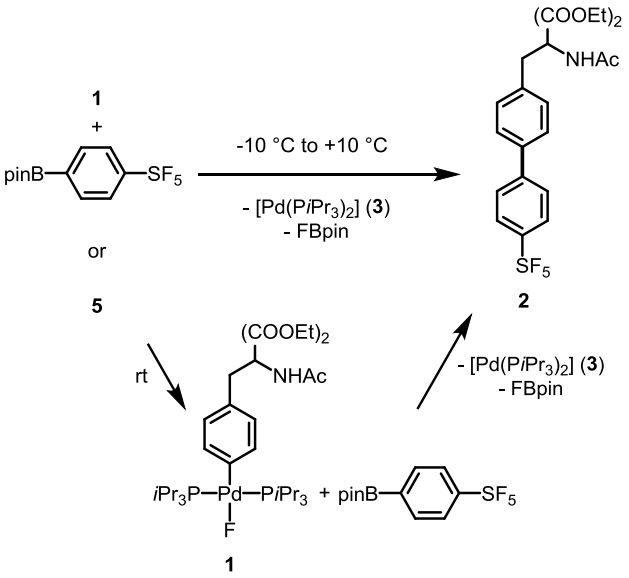
Figure 3. Part of ^{1}H, $^{1}H\{^{19}F\}$ or $^{1}H\{^{31}P\}$ NMR spectra of the reaction of *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) with an excess of $NaBF_4$ at room temperature. **A** Signals for aromatic protons and N*H* of **1** as reference in [D_8]THF. **B** 5 min after addition of $NaBF_4$ to a solution of **1** in [D_8]THF. **C**-**E** Signals for aromatic protons and N*H* of *trans*-[Pd(BF_4)(Phe^{Et})(P*i*Pr$_3$)$_2$] (**7**) and [P*i*Pr$_3$Phe^{Et}][BF_4] (**4**). Signals for **7** are broadened also in $^{1}H\{^{19}F\}$ and $^{1}H\{^{31}P\}$ NMR spectra. **F** [P*i*Pr$_3$Phe^{Et}][BF_4] (**4**) as single phenylalanine derivative obtained as reaction product. # Toluene from the synthesis of **1**.



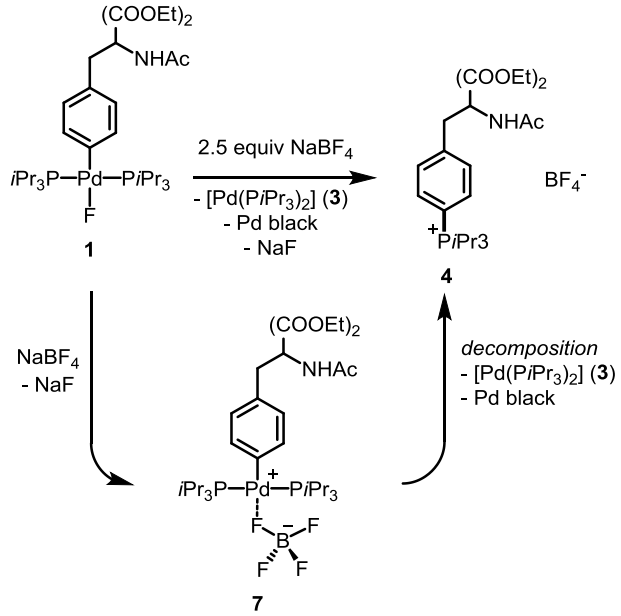
Scheme 1. Reaction of *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) with 4-BpinC$_6$H$_4$SF$_5$ at room temperature. [4-P*i*Pr$_3$Phe^{Et}][BF_4] (**4**) was formed as minor product in addition to the cross-coupling product **2** (ratio 1:8).



Scheme 2. Reversible formation of the ionic intermediate *trans*-[Pd{BF(4-C$_6$H$_4$SF$_5$)(pin)}(Phe^{Et})(P*i*Pr$_3$)$_2$] (**5**) at low temperatures.



Scheme 3. Reaction of *trans*-[PdF(Phe^{Et})(P*i*Pr$_3$)$_2$] (**1**) with 4-BpinC$_6$H$_4$SF$_5$ or *trans*-[Pd{BF(4-C$_6$H$_4$SF$_5$)(pin)}(Phe^{Et})(P*i*Pr$_3$)$_2$] (**5**).



Scheme 4. Formation and degradation of the cationic complex **7**.