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Nickel fluoro complexes as intermediates in catalytic cross-coupling reactions

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ABSTRACT

The C–F activation of pentafluoropyridine or 2,3,5,6-tetrafluoropyridine at [Ni(COD)$_2$] (COD = 1,5-cyclooctadiene) in the presence of ^{i}Pr$_2$PCH$_2$CH$_2$OMe resulted in the formation of the nickel(II) fluoro bisphosphine complexes *trans*-[Ni(F)(2-C$_5$NF$_4$){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**1**), *trans*-[Ni(F)(4-C$_5$NF$_4$){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**2**) and *trans*-[Ni(F)(2-C$_5$NHF$_3$){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**3**). The employment of ^{i}Pr$_2$PCH$_2$CH$_2$NMe$_2$ gave the nickel(II) fluoro monophosphine complexes [Ni(F)(2-C$_5$NF$_4$){κ^2-(*P*,*N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**4**), [Ni(F)(4-C$_5$NF$_4$){κ^2-(*P*,*N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**5**) and [Ni(F)(2-C$_5$NHF$_3$){κ^2-(*P*,*N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**6**) instead, in which the amino moiety coordinates at the metal center. In catalytic experiments pentafluoropyridine could be converted into 3,5,6-trifluorodiphenylpyridine (**7**) and 3,5-difluoro-2,4,6-triphenylpyridine (**8**) in the presence of PhB(OH)$_2$ and 5 mol% of a mixture of **1** and **2** (ratio 8:1) or **5** and **4** (ratio 2:1) as catalysts. Additionally 2,3,5,6-tetrafluoropyridine could be converted catalytically into 3,5-difluoro-2,6-diarylpyridines (**9**: aryl = Ph; **10**: aryl = Tol; **11**: aryl = 4-(F$_3$C)C$_6$H$_5$; **12**: aryl = 4-MeOC$_6$H$_5$) in the presence of boronic acids when 5 mol% of **3** was employed as catalyst.

1. Introduction

Fluorinated building blocks are of considerable significance for a variety of functional compounds such as for example pharmaceuticals, agrochemicals or advanced materials [1]. A possible strategy to access unique fluorinated moieties is represented by a transition-metal mediated derivatization of easily available highly fluorinated precursors. Such reaction pathways can involve C–F activation steps, e.g. at palladium, nickel or rhodium [2–17]. Thus, hydrodefluorination or cross coupling reactions can provide fluorinated building blocks, which are often not accessible otherwise [3–31]. However, catalytic C–F bond functionalization reactions of highly fluorinated aromatic precursors via cross coupling reactions are still rare [4,14,17,23–25,32–47]. Radius et al. reported an initial and exceptional example of a nickel-mediated Suzuki–Miyaura cross coupling reaction of perfluorotoluene with aryl boronic acids on using a nickel(II) carbene complex as catalyst [25]. Sandford et al. demonstrated that [Pd(PPh$_3$)$_4$] catalyses the derivatization of the electron-poor polyfluoronitrobenzene with aryl boronic acids and esters [17]. In a recent example, Love et al. described the application of [(Me)$_2$Pt(μ-SMe$_2$)$_2$]$_2$ or [Ni(COD)$_2$]/PPh$_3$ as precatalysts for the functionalization of polyfluorinated arylimines on using boronic acids [39,47].

There is some precedent in the literature which suggests that complexes bearing hemilabile coordinating ligands can catalyse cross-coupling reactions in a more efficient way than related monodentate counterparts [48]. Thus, Milstein et al. compared the ligand properties of the hemilabile coordinating phosphine di-*tert*-butyl(2,6-dimethoxybenzyl)phosphine (dmobp) with these of di-*tert*-butyl-(2,4,6-trimethylbenzyl)phosphine (tmbp) [49]. They studied the catalytic activity of [Pd(dmobp)$_2$] and [Pd(tmbp)$_2$] in Suzuki–Miyaura coupling reactions of arylchlorides and found that [Pd(dmobp)$_2$] is much more effective than [Pd(tmbp)$_2$]. Also Stradiotto et al. demonstrated that [Pd(cinnamyl)Cl]$_2$/2-(di-*tert*-butylphosphino)-*N*,*N*-dimethylaniline represents a highly versatile catalytic system for the coupling of aryl chlorides with amines. In contrast the use of di-*tert*-butyl-(2-*iso*propylphenyl)phosphine, which does not bear any hemilabile coordinating moiety, resulted in much lower yields [50]. We recently reported that *trans*-[Pd(F)(4-C$_5$NF$_4$){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] catalyses the hydrodefluorination and cross-coupling reaction of pentafluoropyridine to give 2,3,5,6-tetrafluoropyridine or 4-phenyltetrafluoropyridine, respectively [51].

In this work we present studies on the C–F oxidative addition of pentafluoropyridine and 2,3,5,6-tetrafluoropyridine at [Ni(COD)$_2$] in the presence of the phosphines ^{i}Pr$_2$PCH$_2$CH$_2$OMe and ^{i}Pr$_2$PCH$_2$CH$_2$NMe$_2$. Furthermore, we studied the catalytic activity of the resulting nickel(II) fluoro complexes towards cross coupling reactions of the fluorinated heterocycles with boronic acids.

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2. Results

2.1. C–F activation at [Ni(COD)$_2$] in the presence of ^{i}Pr$_2$PCH$_2$CH$_2$OMe

A reaction of [Ni(COD)$_2$] with an excess of ^{i}Pr$_2$PCH$_2$CH$_2$OMe and pentafluoropyridine at room temperature in *n*-hexane led to a C–F activation at the 2- and 4-position to yield the nickel fluoro complexes *trans*-[Ni(F)(2-C$_5$NF$_4$){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**1**) and *trans*-[Ni(F)(4-C$_5$NF$_4$){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**2**) in a ratio of 8:1 (Scheme 1). The use of THF instead of *n*-hexane as a solvent has no influence of the observed ratio of the products [26]. Treatment of [Ni(COD)$_2$] with one equivalent ^{i}Pr$_2$PCH$_2$CH$_2$OMe and pentafluoropyridine gives nearly the same ratio of products, but in considerable lower yields.

The structure which is proposed for **1** is supported by the ^{31}P{^{1}H}, ^{19}F and ^{1}H NMR data. The ^{31}P{^{1}H} NMR spectrum exhibits a doublet at δ 21.7 with a coupling of $^2J_{PF}$ = 44 Hz between the phosphorus atoms and the metal-bound fluorine. The ^{19}F NMR spectrum shows five signals. The signal at δ −376.2 ($^2J_{PF}$ = 44 Hz, J_{FF} = 8 Hz) is characteristic for the fluoro ligand at the metal center [6,23,27,28,52–57]. The assignment of **1** as a 2-tetrafluoropyridyl nickel derivative is based on the presence of four signals of equal integration at δ −86.0, −130.6, −151.8 and −174.0 in the ^{19}F NMR spectrum. The ^{1}H NMR spectrum shows the expected signals for the metal-bonded phosphines. Complex **2** was identified by its ^{31}P{^{1}H}, ^{19}F NMR data. The ^{31}P NMR spectrum displays a doublet at δ 21.1 with a coupling constant of $^2J_{PF}$ = 44 Hz. The ^{19}F NMR spectrum reveals two signals at δ −91.6 and −109 for the fluorine atoms bound at the tetrafluoropyridyl ligand and a triplet of doublets at δ −372.2 ($^2J_{PF}$ = 44 Hz, J_{FF} = 6 Hz) for the metal-bond fluorine.

Addition of ^{i}Pr$_2$PCH$_2$CH$_2$OMe and 2,3,5,6-tetrafluoropyridine to [Ni(COD)$_2$] in *n*-hexane gave the C–F activation product *trans*-[Ni(F)(2-C$_5$NHF$_3$){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**3**) after 4 h. Complex **3** was characterized by its ^{31}P{^{1}H} and ^{19}F NMR data. The presence of four signals in the ^{19}F NMR spectrum is indicative for the trifluoropyridyl ligand (δ −91.6, −109.3, −151.9) with the nickel at the *ortho* position as well as for the metal-bond fluorine (δ −372.4). The ^{31}P{^{1}H} NMR spectrum of complex **3** shows a doublet at δ 21.1 with a coupling constant of $^2J_{PF}$ = 44 Hz. The molecular structure of **3** was also confirmed by X-ray crystallography. Complex **3** was crystallized from *n*-hexane at 0 °C and the molecular structure of one of the two crystallographically independent molecules is depicted in Fig. 1.

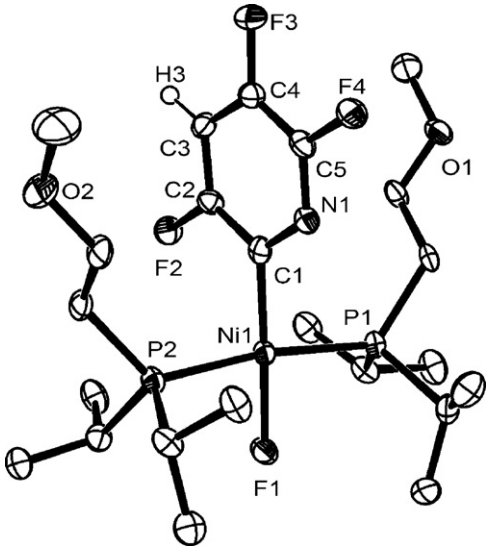
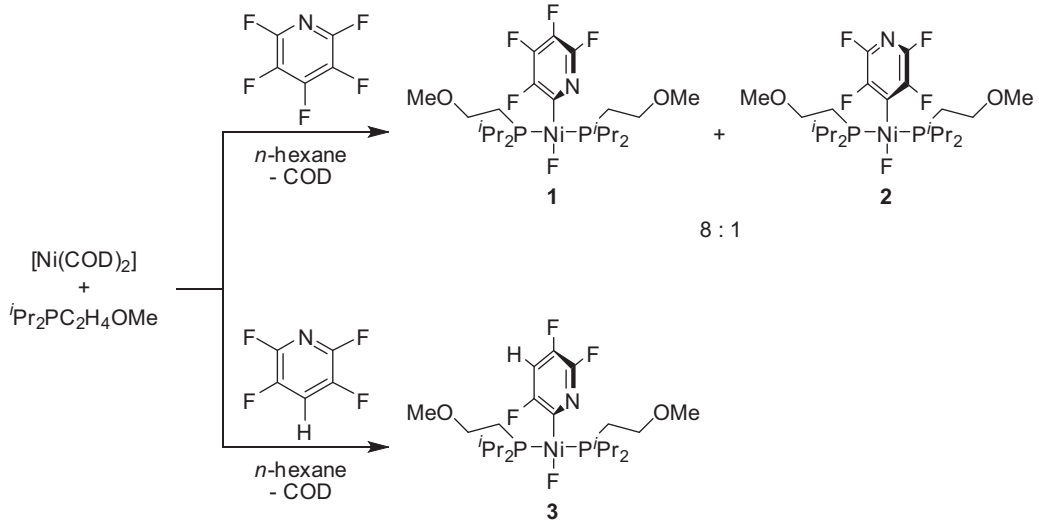


Fig. 1. An ORTEP diagram of **3**; ellipsoids are drawn at the 50% probability level; hydrogen atoms, with the exception of H(3), are omitted for clarity; only one of two crystallographically independent molecules is shown.

Compound **3** crystallizes in the space group $P\,2_12_12_1$. Selected bond lengths and angles are summarized in Table 1. Complex **3** reveals a distorted square-planar structure at the Ni center, with a *trans* configuration of the phosphines as well as of the trifluoropyridyl and the fluoro ligands. The angles at Ni vary from 86.34(11)° to 94.42(15)°. The nickel-fluorine distance in **3** is 1.862(3) Å. For comparison, the Ni–F length in *trans*-[Ni(F)(2-C$_5$NHF$_3$)(PEt$_3$)$_2$] is 1.856(2) Å, and the one in *trans*-[Ni(F)(C$_6$F$_5$)(-PEt$_3$)$_2$] is 1.836(5) Å [52].

2.2. C–F activation at [Ni(COD)$_2$] in the presence of ^{i}Pr$_2$PCH$_2$CH$_2$NMe$_2$.

Treatment of [Ni(COD)$_2$] with ^{i}Pr$_2$PCH$_2$CH$_2$NMe$_2$ and subsequent addition of pentafluoropyridine resulted in the formation of a yellow precipitate, which consisted of [Ni(F)(2-C$_5$NF$_4$){κ^2-(*P*,*N*)-*i*Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**4**) and [Ni(F)(4-C$_5$NF$_4$){κ^2-(*P*,*N*)-*i*Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**5**) in a ratio of 1:2 (Scheme 2). The two complexes were identified as nickel fluoro monophosphine complexes on the basis of doublets ($^2J_{PF}$ = 117 Hz) in the ^{19}F



Scheme 1. C–F activation of fluorinated pyridines at [Ni(COD)$_2$]/^{i}Pr$_2$PCH$_2$CH$_2$OMe.

Table 1
Selected bond lengths (Å) and angles (°) in **3** with the estimated standard deviations in parentheses.

Bond	Length	Bond	Length
Ni(1)–C(1)	1.875 (5)	C(2)–C(3)	1.384 (7)
Ni(1)–F(1)	1.862 (3)	C(3)–C(4)	1.379 (8)
Ni(1)–P(1)	2.2120 (15)	C(4)–C(5)	1.374 (8)
Ni(1)–P(2)	2.2123 (14)	C(5)–F(4)	1.337 (6)
N(1)–C(1)	1.352 (6)	C(2)–F(2)	1.358 (6)
N(1)–C(5)	1.323 (7)	C(4)–F(3)	1.352 (6)
C(1)–C(2)	1.391 (7)		
Bonds	**Angle**	**Bonds**	**Angle**
C(1)–Ni(1)–P(1)	94.42 (15)	C(5)–N(1)–C(1)	119.4 (5)
F(1)–Ni(1)–P(2)	86.34 (11)	N(1)–C(1)–C(2)	117.8 (5)
C(1)–Ni(1)–F(1)	176.3 (2)	C(3)–C(2)–C(1)	123.9 (5)
P(1)–Ni(1)–P(2)	171.04 (6)	C(4)–C(3)–C(2)	115.4 (5)
N(1)–C(1)–Ni(1)	120.3 (4)	C(5)–C(4)–C(3)	119.6 (5)
C(2)–C(1)–Ni(1)	121.8 (4)	N(1)–C(5)–C(4)	123.9 (5)

NMR spectrum at δ −294.7 and δ −313.4. The coupling constants indicate a *trans* position of the fluoro ligands and the phosphine moieties. The 4-pyridyl isomer [Ni(F)(4-C_5NF_4){κ^2-(*P,N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**5**) exhibits two multiplets in the ^{19}F NMR spectrum at δ −99.9 and −123.1 for the tetrafluoropyridyl ligand with the nickel at the 4-position. The ^{31}P{^{1}H} NMR spectrum shows a doublet at δ 61.0 ($^2J_{P,F}$ = 117 Hz). The 2-pyridyl complex **4** was also characterized by its ^{19}F, ^{31}P{^{1}H} NMR data. The ^{31}P{^{1}H} NMR spectrum of **4** exhibits a doublet at δ 61.0 ($^2J_{PF}$ = 117 Hz), whereas the ^{19}F NMR spectrum shows four resonances for the tetrafluoropyridyl ligand at δ −88.6, −132.6, −150.8 and −172.5.

The molecular structure of **5** was also confirmed by X-ray crystallography (Fig. 2 and Table 2). Complex **5** was crystallized by gas phase diffusion of *n*-hexane into a saturated THF solution. The unit cell contains two crystallographically independent molecules. However, one of the moieties is a superposition of **4** and **5**, which will not be discussed further. The molecular structure of **5** confirms the expected *trans* disposition of the fluoro ligand and the phosphorus atom and reveals a distorted square-planar coordination geometry at the metal center. The angles about the nickel atom vary from 87.53(9)° to 94.69(8)°. The Ni(1)–F(1) distance of 1.8383(14) Å and the Ni(1)–C(11) distance to the tetrafluoropyridyl ligand of

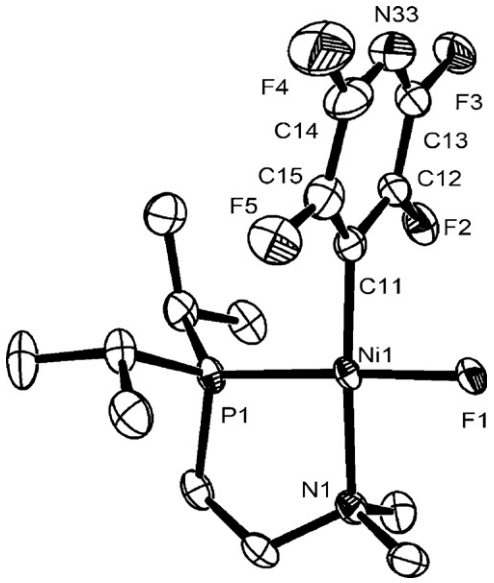
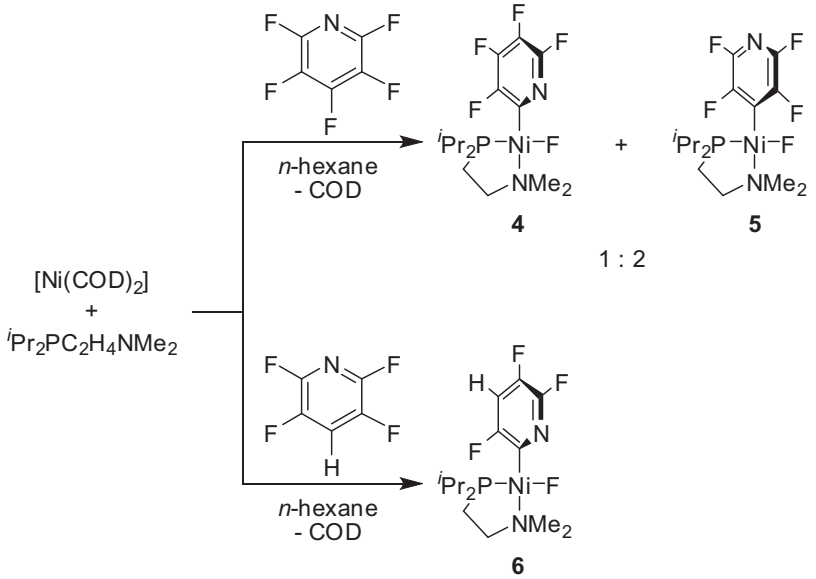


Fig. 2. An ORTEP diagram of **5**; ellipsoids are drawn at the 50% probability level; hydrogen atoms are omitted for clarity.

1.892(3) Å are in a similar range as the corresponding separations in [Ni(F)(2-C_5NF_4)($Cy_2PCH_2CH_2PCy_2$)] (Ni–F = 1.8473(12) Å, Ni–C = 1.917(2) Å) [26].

The activation of a fluorinated pyridine at the 2-position was also found when *i*Pr$_2$PCH$_2$CH$_2$NMe$_2$ and 2,3,5,6-tetrafluoropyridine were added to a solution of [Ni(COD)$_2$] in *n*-hexane at room temperature. After 1 h the formation of the fluoro complex [Ni(F)(2-C_5NHF_3){κ^2-(*P,N*)-*i*Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**6**) was observed (Scheme 2), which was characterized by its NMR spectroscopic data. The ^{19}F NMR spectrum shows three signals at δ −93.3, −109.8 and −149.9, which indicate the presence of the trifluoropyridyl ligand with the nickel center at the 2-position of the heterocycle. The doublet at δ −292.2 ($^2J_{PF}$ = 120 Hz) results from the metal-bonded fluorine in the *trans* position to the phosphorus atom. The ^{31}P{^{1}H} NMR spectrum exhibits a doublet at δ −61.4 ($^2J_{PF}$ = 120 Hz).

Complex **6** was crystallized from gas phase diffusion of *n*-hexane into a solution of wet THF. The yellow crystals were



Scheme 2. C–F activation of fluorinated pyridines at [Ni(COD)$_2$]/^{i}Pr$_2$PCH$_2$CH$_2$NMe$_2$.

Table 2
Selected bond lengths (Å) and angles (°) in **5** with the estimated standard deviations in parentheses.

Bond	Length	Bond	Length
Ni(1)–C(11)	1.892 (3)	C(12)–F(2)	1.346 (3)
Ni(1)–F(1)	1.8383 (14)	C(13)–F(3)	1.347 (4)
Ni(1)–N(1)	1.992 (2)	C(14)–F(4)	1.349 (4)
Ni(1)–P(1)	2.1251 (7)	C(15)–F(5)	1.322 (4)
Bonds	**Angle**	**Bonds**	**Angle**
C(11)–Ni(1)–N(1)	176.71 (9)	C(15)–C(11)–C(12)	113.1 (3)
F(1)–Ni(1)–P(1)	177.06 (6)	C(13)–C(12)–C(11)	121.7 (3)
C(11)–Ni(1)–P(1)	94.69 (8)	N(33)–C(13)–C(12)	124.7 (3)
C(11)–Ni(1)–F(1)	87.53 (9)	N(33)–C(14)–C(15)	124.7 (3)
N(1)–C(1)–C(2)	111.5 (2)	C(11)–C(15)–C(14)	120.5 (3)
C(1)–C(2)–P(1)	107.76 (17)	C(13)–N(33)–C(14)	115.2 (3)

Table 3
Selected bond lengths (Å) and angles (°) in **6** with the estimated standard deviations in parentheses.

Bond	Length	Bond	Length
Ni(1)–C(1)	1.348 (6)	C(2)–F(2)	1.364 (5)
Ni(1)–F(1)	1.876 (3)	C(5)–F(4)	1.353 (5)
Ni(1)–P(1)	2.1122 (12)	F(1)–H(102^{i})	1.7236 (36)
Ni(1)–N(2)	1.999 (4)	F(1)–O(1^{i})	2.6740 (62)
Bonds	**Angle**	**Bonds**	**Angle**
C(1)–Ni(1)–P(1)	90.85 (13)	C(4)–C(3)–C(2)	114.9 (4)
F(1)–Ni(1)–P(1)	91.62 (15)	C(3)–C(2)–C(1)	124.5 (4)
F(1)–Ni(1)–N(2)	89.48 (15)	N(1)–C(1)–C(2)	117.9 (4)
C(1)–Ni(1)–N(2)	172.1 (2)	C(5)–N(1)–C(1)	118.7 (4)

suitable for X-ray diffraction analysis (Fig. 3 and Table 3). The unit cell contains two crystallographically independent molecules that exhibit only minor structural differences, but both exhibit a hydrogen bridge to the same water molecule. However, only one molecule will be discussed. Complex **6** crystallized in the space group $P\,2_1$. It exhibits a square-planar structure at Ni with the fluoro ligand coordinated in the *trans* position to the phosphorus atom. The angles about the nickel atom are distorted from an ideal square-planar geometry and vary from 89.48(15)° to 91.62(15)°. The nickel fluoro bond in **6** of 1.876(3) Å is similar to the corresponding distances in **3** and **4**. The F–O separation F(1)–O(1^{i}) of 2.6740(62) Å indicates that the additional water molecule in the cell is bound to **6** via a hydrogen bond to the fluoro ligand. Comparable hydrogen–fluoro interactions have been observed before for other metal fluoro complexes [20,26,28,53,58].

2.3. Catalytic cross-coupling reactions of pentafluoropyridine

Treatment of pentafluoropyridine with phenyl boronic acid in the presence of 5 mol% of a mixture of *trans*-[Ni(F)(2-C_5NF_4){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**1**) and *trans*-[Ni(F)(4-C_5NF_4){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**2**) (ratio: 8:1) and NEt_3 as base gave the C–C coupling products 3,4,5-trifluoro-2,6-biphenylpyridine (**7**) and 3,5-difluoro-2,4,6-triphenylpyridine (**8**) with yields of 20% and 10% after 17 h at 60 °C (Scheme 3 and Table 4). In addition, the formation of traces of 3,5-difluoro-2,6-biphenylpyridine (**9**) and 2,3,5,6-tetrafluoropyridine was observed. A mixture of the complexes **5** and **4** (ratio: 2:1) also shows catalytic activity in cross coupling reactions. In contrast to the reaction above only the formation of **8** was observed (Scheme 3). We did not observe any reaction of $PhB(OH)_2$ with pentafluoropyridine without adding a nickel fluoro complex, even in the presence of NEt_3. To the best of our knowledge only **8** is known in the literature [59]. The pyridines **7** and **9** were identified by their mass spectra and ^{19}F NMR spectroscopic data (Table 5).

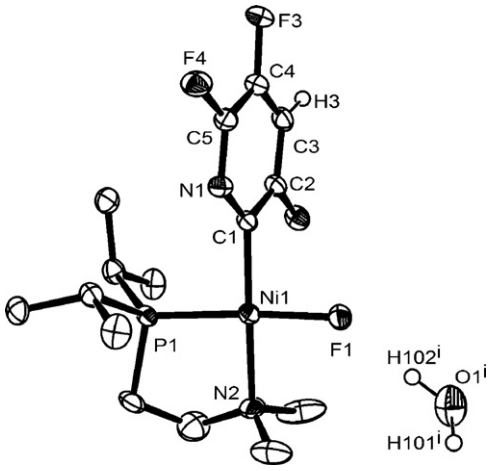


Fig. 3. An ORTEP diagram of **6**; ellipsoids are drawn at the 50% probability level; hydrogen atoms at the nickel complex, with the exception of H(3), are omitted for clarity.

Note that the use of Cs_2CO_3 as base instead of NEt_3 afforded the same products in lower yields for the use of **1** and **2** (ratio 8:1) and **5** and **4** (ratio 2:1) as catalysts. In addition the formation of second product was observed which we tentatively assign as Cs[(4-OC_5NF_4)]. The same compound was formed in an NMR experiment in a reaction of Cs_2CO_3 with pentafluoropyridine at 60 °C and was identified by its ^{19}F NMR spectroscopic data [δ (THF-d_8): −102.6 (m, 2F), −172.0 (m, 2F)] and its mass spectrum.

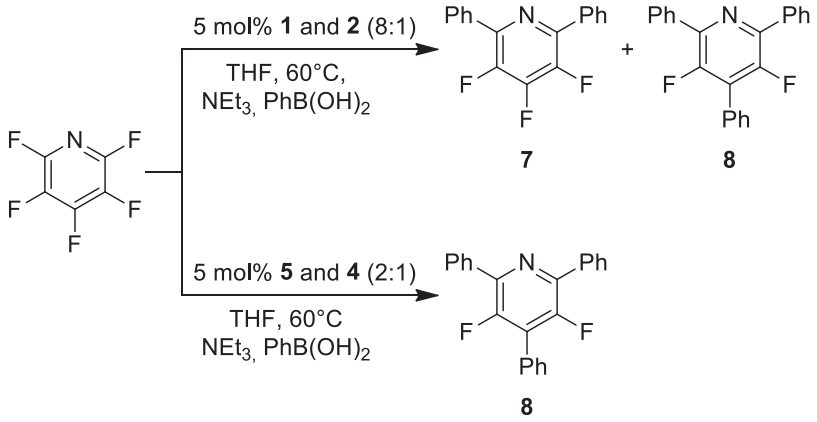
2.4. Catalytic cross-coupling reactions of 2,3,5,6-tetrafluoropyridine

Treatment of 2,3,5,6-tetrafluoropyridine with boronic acids in the presence of 5 mol% *trans*-[Ni(F)(2-C_5NHF_3){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**3**) as a catalyst and a base afforded at 60 °C with high regioselectively 3,5-difluoro-2,6-di(aryl)pyridines (**9**: aryl = Ph; **10**: aryl = Tol; **11**: aryl = 4-(F$_3$C)C$_6$H$_5$; **12**: aryl = 4-MeOC$_6$H$_5$) in 95–99% yield. Representative results are summarized in Scheme 4 and Table 6.

The influence of several bases such as KF, Et_3N or Cs_2CO_3 was tested for the formation of **9**. We found that Cs_2CO_3 led to the highest yield and the other reactions were, therefore, performed in the presence of Cs_2CO_3 (Table 6). The compounds **9**–**12** have not been described before and were characterized by their ^{19}F NMR spectroscopic data (Table 5) and ESI-MS. Employment of [Ni(F)(2-C_5NF_4){κ^2-(*P,N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**6**) as catalyst also yielded with phenyl boronic acid the diaryl pyridine **9**, but in lower yields. We did not observe any reaction of $PhB(OH)_2$ with 2,3,5,6-tetrafluoropyridine without adding a nickel fluoro complex, even in the presence of Cs_2CO_3.

3. Discussion

The syntheses of the isomeric nickel fluoro complexes *trans*-[Ni(F)(2-C_5NF_4){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**1**) and *trans*-[Ni(F)(4-C_5NF_4){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**2**) are shown in Scheme 1. Comparable oxidative addition reactions at nickel bisphosphine moieties are known in the literature [6,26,27,52–54,56]. Note that for the C–F activation step several mechanism have been discussed [3,6,26]. A phosphine-assisted mechanism has been suggested, and comparable reaction pathways were found at rhodium, iridium and platinum [16,19,60,61]. However, Johnson et al. suggested a concerted oxidative addition for the activation of 2,3,5,6-tetrafluoropyridine at [Ni(η^2-$C_{14}H_{10}$)(PEt$_3$)$_2$] [62]. For the C–F activation of pentafluoropyridine they discussed a radical mechanism.



Scheme 3. Catalytic cross-coupling reactions of pentafluoropyridine.

Table 4
Cross-coupling reactions of pentafluoropyridine with phenyl boronic acid.

Entry	Cat.	Product	Yield (%)	TON	Product	Yield (%)	TON
1	**1**+**2**[a]	**7**	20	8	**8**	10	6
2	**5**+**4**[b]	**7**	–	–	**8**	13	8

5 mol% of catalyst ([a]ratio of 8:1; [b]ratio of 2:1); Et_3N, THF, 60 °C, 17 h; yields are based on the amounts of pentafluoropyridine and have been determined by ^{19}F NMR spectroscopy on using a capillary which contained α,α,α-trifluorotoluene as external standard; TON, turn-over number.

Table 5
^{19}F NMR data of fluorinated pyridines at 25 °C (ppm).

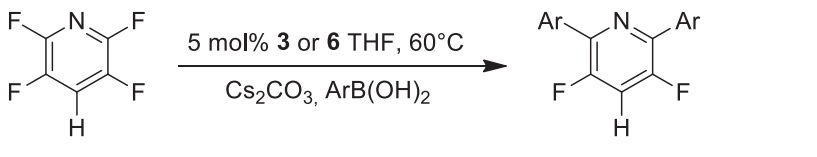
Compound	δ (^{19}F) (THF-d_8)
7	−146.5 (d, 2F, J_{FF} = 19.1 Hz), −148.8 (t, 1F, J_{FF} = 19.1 Hz) [59]
8	−126.5 (s, 2F)
9	−121.5 (s, 2F)
10	−122.1 (s, 2F)
11	−123.0 (s, 2F)
12	−119.4 (s, 2F)

In contrast, the C–F activation of pentafluoropyridine at [Ni(COD)$_2$]/^{i}Pr$_2$PCH$_2$CH$_2$NMe$_2$ (Scheme 3) yields the monophosphine 4-pyridyl complex [Ni(F)(4-C_5NF_4){κ^2-(*P,N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**5**) as the main product and the 2-pyridyl complex [Ni(F)(2-C_5NF_4){κ^2-(*P,N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**4**) as the minor product. In these cases the phosphine coordinates with both donor atoms (P,N) at the nickel center. Treatment of **5** with an excess of ^{i}Pr$_2$PCH$_2$CH$_2$NMe$_2$ does not afford the formation of a bisphosphine complex. Note that the formation of [Ni(F)(2-C_5NF_4)(Cy$_2$PCH$_2$CH$_2$PCy$_2$)] and [Ni(F)(2-C_5NF_4)(^{t}Bu$_2$PCH$_2$CH$_2$P^{t}Bu$_2$)] has been observed, which also exhibit a *cis* configuration of a fluoro- and a fluoroaryl ligand [26,63].

In general, there is a preference for the activation of pentafluoropyridine at the 4-position at a variety of transition metal complexes [20,33,51,64,65]. For instance, at palladium the generation of *trans*-[Pd(F)(4-C_5NF_4)(PR$_3$)$_2$] (PR$_3$ = PCy$_3$, P^{i}Pr$_3$, ^{i}Pr$_2$PCH$_2$CH$_2$OMe) was observed [20,51]. Other examples involve the formation of [Ru(ICy)(dppp)(CO)(4-C_5NF_4)(H)] [dppp = 1,4-bis(diphenylphosphanyl)propane], [Rh(4-C_5NF_4)(PEt$_3$)$_3$] or [Pt(4-C_5NF_4)(^{i}Pr)(P^{i}Pr$_3$)(PF^{i}Pr$_2$)] [20,33,64]. Activation reactions at the 2-position involve reactions at nickel to yield *trans*-[Ni(F)(2-C_5NF_4)(L)$_2$] (L = PEt$_3$, ^{i}Pr$_2$Im), at rhodium to give [Rh(2-C_5NF_4)(PEt$_3$)$_3$], but also conversions at titanium and zirconium [16,19,26,28,29,52,62,66].

The activation of 2,3,5,6-tetrafluoropyridine at [Ni(COD)$_2$] proceeds in the presence of both phosphines, ^{i}Pr$_2$PCH$_2$CH$_2$OMe or ^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$, at the 2-position (Schemes 1 and 2) and yielded *trans*-[Ni(F)(2-C_5NHF_3){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**3**) and [Ni(F)(2-C_5NHF_3){κ^2-(*P,N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**6**). In both cases the C–F activation is favored over the C–H activation. The activation of a C–F bond in the presence of a C–H bond was observed before at nickel bisphosphine complexes [6,52,54,67]. The formation of the nickel fluoro complexes is presumably thermodynamically favored whereas the formation of the C–H activation products seem to be kinetically preferred [57,62,67,68]. Recently Johnson et al. reported an experimental study of the C–F activation of 2,3,5,6-tetrafluoropyridin at a Ni(PEt$_3$)$_2$ synthon to yield *trans*-[Ni(F)(2-C_5NHF_3)(PEt$_3$)$_2$]. At low temperature they observed the formation of the kinetically favored nickel hydrido complex *trans*-[Ni(H)(4-C_5NF_4)(PEt$_3$)$_2$] [62].

The C–F activation reactions are key-steps for the development of catalytic processes such as C–C coupling reactions access new fluoropyridines. The nickel fluoro complexes which have been synthesized can be considered as essential intermediates of a putative catalytic cycle. Note that it has been shown before that fluoro complexes often exhibit a higher reactivity than their chloro or bromo counterparts [18,19,21–29,31,51,69]. Representative results of the cross coupling reactions of pentafluoropyridine



9: Ar = Ph
10: Ar = Tol
11: Ar = 4-(MeO)C_6H_5
12: Ar = 4-(CF_3)C_6H_5

Scheme 4. Catalytic cross-coupling reactions of 2,3,5,6-tetrafluoropyridine.

Table 6
Cross-coupling reactions of 2,3,5,6-tetrafluoropyridine with boronic acids.

Entry	Boronic acid	Product	Base	Yield (%)	TON
1	$PhB(OH)_2$	**9**	NEt_3	62[a]	25
2	$PhB(OH)_2$	**9**	KF	47[a]	19
3	$PhB(OH)_2$	**9**	Cs_2CO_3	99[a]	40
4	$PhB(OH)_2$	**9**	Cs_2CO_3	17[b]	7
5	$TolB(OH)_2$	**10**	Cs_2CO_3	98[a]	39
6	4-$(F_3C)C_6H_5$	**11**	Cs_2CO_3	95[a]	38
7	4-$(MeO)C_6H_5$	**12**	Cs_2CO_3	97[a]	39

Yields are based on the amounts of 2,3,5,6-tetrafluoropyridine and have been determined by ^{19}F NMR spectroscopy on using a capillary which contained fluorobenzene[a] or α,α,α-trifluorotoluene[b] as external standard; TON, turn-over number.
[a] 5 mol% of **3**, THF, 60 °C, 3 h.
[b] 5 mol% of **6**, THF, 60 °C, 3 d.

and 2,3,5,6-tetrafluoropyridine as substrates are summarized in Schemes 3 and 4. For the former 2,6-diaryl- as well as 2,4,6-triarylpyridines were generated. For the latter substrate the bisphosphine complex *trans*-[Ni(F)(2-C_5NF_4){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**3**) is superior as a catalyst in comparison to the nickel fluoro monophosphine complex [Ni(F)(2-C_5NHF_3){κ^2-(*P*,*N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**6**). Some rare examples for cross-coupling reactions that involve the cleavage of a C–F bond at highly fluorinated aromatics have been reported [4,14,17,21,23–25,32–47,51,70]. Chambers and Sandford described palladium catalysed Suzuki cross-coupling reactions via C–Br activation of 2,4,6-tribromo-3,5-difluoropyridine and aromatic boronic acids. They also observed a threefold or twofold substitution at the pyridine, in this case by C−Br activation [59].

4. Summary

In conclusion, we presented studies on the synthesis and catalytic activity of the nickel fluoro complexes *trans*-[Ni(F)(2-C_5NF_4){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**1**), *trans*-[Ni(F)(4-C_5NF_4){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**2**), *trans*-[Ni(F)(2-C_5NF_4){κ^1-(*P*)-(^{i}Pr$_2$*P*CH$_2$CH$_2$OMe)$_2$}] (**3**), [Ni(F)(2-C_5NHF_3){κ^2-(*P*,*N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**4**), [Ni(F)(4-C_5NHF_3){κ^2-(*P*,*N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**5**) and [Ni(F)(2-C_5NF_4){κ^2-(*P*,*N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**6**). All complexes can be synthesized by carbon-fluorine-bond activation of pentafluoropyridine or 2,3,5,6-tetrafluoropyridine. Via catalytic cross-coupling reactions with pentafluoropyridine several new fluorinated building blocks have been accessed by C–F activation. Complex **3** catalyses a twofold C–F activation at 2,3,5,6-tetrafluoropyridine to yield the new 3,5-difluoro-2,6-di(aryl)-pyridines (**9**: aryl = Ph; **10**: aryl = Tol; **11**: aryl = 4-$(F_3C)C_6H_5$; **12**: aryl = 4-$MeOC_6H_5$).

5. Experimental

5.1. General

The synthetic work was carried out on a Schlenk line under Ar. All solvents were purified and dried by conventional methods and distilled under argon before use. Benzene-d_6 and THF-d_8 were dried over Na/K prior to use. [Ni(COD)$_2$], ^{i}Pr$_2$PCH$_2$CH$_2$OMe and ^{i}Pr$_2$PCH$_2$CH$_2$NMe$_2$ were prepared according to the literature [71].

The NMR spectra were recorded at 300 K at a Bruker DPX 300 spectrometer. The ^1H NMR chemical shifts were referenced to residual C_6D_5H at 7.15 ppm, THF-d_7 at 1.72 ppm or at 3.58 ppm. The ^{19}F NMR spectra were referenced to external C_6F_6 at −162.9 ppm. The $^{31}P\{^1H\}$ NMR spectra were referenced externally to H_3PO_4 at 0.0 ppm. Microanalyses were carried out using a *HEKAtech* EURO EA 3000 elemental analyzer. Mass spectra (ESI) were recorded on an *Agilent* 6210 Time-of-Fight LC–MS instrument.

5.2. Synthesis of trans-[Ni(F)(2-C_5NF_4){κ^1-(P)-(^{i}Pr$_2$PCH$_2$CH$_2$OMe)$_2$}] (**1**) and trans-[Ni(F)(4-C_5NF_4){κ^1-(P)-(^{i}Pr$_2$PCH$_2$CH$_2$OMe)$_2$}] (**2**).

A solution of [Ni(COD)$_2$] (391 mg, 1.43 mmol) in THF (5 mL) was treated with ^{i}Pr$_2$PCH$_2$CH$_2$OMe (1.20 mL, 6.42 mmol). After stirring the reaction mixture for 30 min, pentafluoropyridine (0.19 mL, 1.85 mmol) was added. The reaction mixture was stirred for another 3.5 h and the volatiles were removed under vacuum. The remaining dark red oil was washed with *n*-hexane (4× 5 mL) at −85 °C. The residue was then extracted with *n*-hexane (5 mL) at room temperature. Evaporation of the solvent from the extract under vacuum yielded a yellow solid. Yield: 593 mg (72%, with a ratio of 8:1 for **2**:**1**). Anal. Calcd. for $C_{23}H_{42}NF_5O_2P_2Ni$: C, 47.61; H, 7.30; N, 2.41. Found: C, 47.89; H, 7.55; N, 2.12.

1: ^1H NMR (300.1 MHz, C_6D_6) δ 1.04 (6 H, dd, $^3J_{PH}$ = 13.2 Hz, $^3J_{HH}$ = 7.2 Hz, PCHC*H*$_3$), 1.13 (6H, dd, $^3J_{PH}$ = 14.0 Hz, $^3J_{HH}$ = 7.1 Hz, PCHC*H*$_3$), 1.33 (6H, dd, $^3J_{PH}$ = 15.6 Hz, $^3J_{HH}$ = 7.1 Hz, PCHC*H*$_3$), 1.38 (6H, dd, $^3J_{PH}$ = 16.1 Hz, $^3J_{HH}$ = 7.2 Hz, PCHC*H*$_3$), 1.50 (4H, m, t in the $^1H\{^{31}P\}$ NMR spectrum, $^3J_{HH}$ = 7.4 Hz, PC*H*$_2$), 1.80 (2H, m, sept in the $^1H\{^{31}P\}$ NMR spectrum, $^3J_{HH}$ = 7.1 Hz, PC*H*), 1.91 (2H, m, sept in the $^1H\{^{31}P\}$ NMR spectrum, $^3J_{HH}$ = 7.1 Hz, PC*H*), 3.09 (6H, s, OC*H*$_3$), 3.48 (4H, m, C*H*$_2$OCH$_3$); the $^3J_{HH}$ coupling constants were confirmed from a $^1H\{^{31}P\}$ NMR spectrum. ^{19}F NMR (282.4 MHz, C_6D_6): δ = −86.0 (1F, td, *J* = 29, *J* = 15 Hz), −130.6 (1F, tm, *J* = 28 Hz), −151.8 (1F, m), −174.0 (1F, m), −376.2 (1F, td, $^2J_{PF}$ = 44 Hz, J_{FF} = 8 Hz). $^{31}P\{^1H\}$ (121.5 MHz, C_6D_6) δ 21.7 (d, $^2J_{PF}$ = 44 Hz).

2: ^{19}F NMR (282.4 MHz, C_6D_6): δ = −91.6 (2F, tm, *J* = 31 Hz), −109.3 (2F, dm, *J* = 31 Hz), −372.2 (1F, td, $^2J_{PF}$ = 44 Hz, J_{FF} = 6 Hz). $^{31}P\{^1H\}$ (121.5 MHz, C_6D_6) δ 21.1 (d, $^2J_{PF}$ = 44 Hz).

5.3. Synthesis of trans-[Ni(F)(2-C_5NHF_3){κ^1-(P)-(^{i}Pr$_2$PCH$_2$CH$_2$OMe)$_2$}] (**3**)

A solution of [Ni(COD)$_2$] (203 mg, 0.741 mmol) in THF (5 mL) was treated with ^{i}Pr$_2$PCH$_2$CH$_2$OMe (623 μL, 3.33 mmol). After stirring the reaction mixture for 30 min, 2,3,5,6-tetrafluoropyridine (102 μL, 1.85 mmol) was added. The reaction mixture was stirred for another 3.5 h and the volatiles were removed under vacuum. The remaining dark red oil was washed with *n*-hexane (4× 5 mL) at −85 °C. The residue was then extracted with *n*-hexane at room temperature. Evaporation of the solvent from the extract under vacuum yielded a yellow solid. Yield: 235 mg (56%). Anal. Calcd. for $C_{23}H_{43}NF_4O_2P_2Ni$: C, 49.13; H, 7.71; N, 2.49. Found: C, 49.28; H, 7.58; N, 2.37. ^1H NMR (300.1 MHz, C_6D_6) δ 1.08 (6H, dd, $^3J_{PH}$ = 13.8 Hz, $^3J_{HH}$ = 7.1 Hz, PCHC*H*$_3$), 1.15 (6H, dd, $^3J_{PH}$ = 14.0 Hz, $^3J_{HH}$ = 7.0 Hz, PCHC*H*$_3$), 1.35 (6H, dd, $^3J_{PH}$ = 14.8 Hz, $^3J_{HH}$ = 7.1 Hz, PCHC*H*$_3$), 1.42 (6H, dd, $^3J_{PH}$ = 15.1 Hz, $^3J_{HH}$ = 7.1 Hz, PCHC*H*$_3$), 1.55 (4H, m, PC*H*$_2$), 1.83 (2H, m, sept in the $^1H\{^{31}P\}$ NMR spectrum, $^3J_{HH}$ = 7.1 Hz, PC*H*), 1.95 (2H, m, sept in the $^1H\{^{31}P\}$ NMR spectrum, $^3J_{HH}$ = 7.0 Hz, PC*H*), 3.10 (s, 6H, OC*H*$_3$), 3.52 (4H, m, C*H*$_2$OCH$_3$), 6.21 (1H, m, C*H*); the $^3J_{HH}$ coupling constants were confirmed from a $^1H\{^{31}P\}$ NMR spectrum. ^{19}F NMR (282.4 MHz, C_6D_6) δ −91.6 (1F, t, *J* = 31 Hz), −109.3 (1F, dm, *J* = 32 Hz), −151.9 (1F, dt, *J* = 30, *J* = 4 Hz), −372.4 (1F, tm, $^2J_{PF}$ = 44 Hz). $^{31}P\{^1H\}$ (121.5 MHz, C_6D_6) δ 21.1 (d, $^2J_{PF}$ = 44 Hz).

5.4. Synthesis of [Ni(F)(2-C_5NF_4){κ^2-(P,N)-^{i}Pr$_2$PCH$_2$CH$_2$NMe$_2$}] (**4**) and [Ni(F)(4-C_5NF_4){κ^2-(P,N)-^{i}Pr$_2$PCH$_2$CH$_2$NMe$_2$}] (**5**)

To a suspension of [Ni(COD)$_2$] (147 mg, 0.53 mmol) in *n*-hexane (12 mL) *i*Pr$_2$PCH$_2$CH$_2$NMe$_2$ (113 μL, 0.53 mmol) was added and the mixture was and stirred for 20 min at room temperature. Within 1 min the yellow solution turned orange. After addition of an excess pentafluoropyridine (71 μL, 0.69 mmol) a yellow solid starts to precipitate. The reaction mixture was stirred for 1 h and filtered. The yellow residue was washed with *n*-hexane (3× 2 mL)

Table 7
Crystallographic data for **3**, **5** and **6**.

Compound	**3**	**5**	**6**
Empirical formula	$C_{23}H_{43}NF_4O_2P_2Ni$	$C_{15}H_{24}N_2F_5PNi$	$C_{30}H_{52}N_4F_8P_2Ni_2\ H_2O$
Formula weight	562.23	417.04	417.09
Crystal dimensions (mm^3)	$0.09 \times 0.05 \times 0.01$	$0.40 \times 0.23 \times 0.15$	$0.90 \times 0.43 \times 0.19$
Crystal system	Orthorhombic	Monoclinic	Monoclinic
Space group	$P\ 2_12_12_1$	$P\ 2_1/c$	$P\ 2_1$
a (Å)	8.4409(4)	19.0669(3)	12.2685(5)
b (Å)	16.8825(5)	9.0499(2)	10.5179(3)
c (Å)	19.5388(6)	21.9130(3)	14.3884(6)
β (°)		101.4790(10)	103.109(3)
V ($Å^3$)	2784.35(18)	3705.53(11)	1808.28(12)
Z	4	8	2
Density (calcd.) ($Mg\,m^{-3}$)	1.341	1.495	1.499
μ(Mo-Kα) (mm^{-1})	0.858	1.180	1.201
θ range (°)	2.08–29.50	2.18–29.50	3.39 to 29.61
Reflections collected	18478	70894	26966
Independent reflections	7743	10325	9640
R_{int}	0.0983	0.0622	0.0883
Goodness-of-fit on F^2	0.996	0.839	1.076
Completeness to max. θ	99.8	100.0	99.2
R_1, wR_2 on all data	0.0938, 0.1682	0.0670, 0.1042	0.0674, 0.1431
R_1, wR_2 [$I_o > 2\sigma(I_o)$]	0.0626, 0.1477	0.0422, 0.0990	0.0674, 0.1431
Reflect. with [$I_o > 2\sigma(I_o)$]	5551	6809	8877
Max diff peak, hole e $Å^{-3}$	0.763 and −1.199	1.186 and −0.459	1.571 and −1.082
CCDC	876294	876295	876296

at 0 °C and dried under vacuum. Yield: 177 mg (80%, with a ratio of 1:2 for **4**:**5**). Anal. Calcd. for $C_{15}H_{24}F_5N_2PNi$: C, 43.20; H, 5.80; N, 6.72. Found: C, 43.24; H, 5.50; N, 6.97.

4: ^{19}F NMR (282.4 MHz, C_6D_6) δ −88.6 (1F, m), −132.6 (1F, t, J = 27 Hz), −150.8 (1F, m), −172.5 (1F, m), −294.7 (1F, d, br, $^2J_{PF}$ = 117 Hz). $^{31}P\{^1H\}$ (121.5 MHz, C_6D_6) δ 61.8 (d, $^2J_{PF}$ = 117 Hz).

5: ^1H NMR (300.1 MHz, C_6D_6) δ = 0.43–0.58 (2H, m, PCH_2), 0.65–0.87 (6H, m, PCHCH_3), 1.38–1.49 (4H, m, CH_2N(CH_3)$_2$, PCHCH_3), 2.13 (6H, s, NCH_3). ^{19}F NMR (282.4 MHz, C_6D_6) δ −99.9 (2F, m), −123.1 (2F, m), −313.4 (1F, d, br, $^2J_{PF}$ = 117 Hz). $^{31}P\{^1H\}$ (121.5 MHz, C_6D_6) δ 61.0 (d, $^2J_{PF}$ = 117 Hz).

5.5. Synthesis of [Ni(F)(2-C_5NHF_3){κ^2-(P,N)-^{i}Pr$_2$PCH$_2$CH$_2$NMe$_2$}] (**6**)

To a suspension of [Ni(COD)$_2$] (60 mg, 0.22 mmol) in *n*-hexane (12 mL) *i*Pr$_2$PCH$_2$CH$_2$NMe$_2$ (46 μL, 0.22 mmol) was added and the mixture was stirred for 20 min at room temperature. Within 1 min the yellow solution turned orange. After addition of 2,3,5,6-tetrafluoropyridin (22 μL, 0.22 mmol) a yellow precipitate formed. The reaction mixture was stirred for 1 h and filtered. The yellow residue was washed with *n*-hexane (3× 2 mL) at 0 °C and dried under vacuum. Yield: 56 mg (64%). Anal. Calcd. for $C_{15}H_{25}F_4N_2PNi$: C, 45.15; H, 6.31; N, 7.02. Found: C, 45.19; H, 6.39; N, 7.05. ^1H NMR (300.1 MHz, C_6D_6) δ = 0.52–0.62 (2H, m, PCH_2), 0.81 (6H, dd, $^3J_{PH}$ = 16 Hz, $^3J_{HH}$ = 7 Hz, PCHCH_3), 0.89 (6H, dd, $^3J_{PH}$ = 16 Hz, $^3J_{HH}$ = 7 Hz, PCHCH_3), 1.43–1.54 (4H, m, CH_2N(CH_3)$_2$, PCHCH_3), 2.18 (6H, s, NCH_3), 6.23–6.31 (1H, m, CH); the $^3J_{HH}$ coupling constants were confirmed from a $^1H\{^{31}P\}$ NMR spectrum. ^{19}F NMR (282.4 MHz, C_6D_6) δ −93.3 (1F, t, J = 30 Hz), −109.8 (1F, d, J = 31 Hz), −149.9 (1F, d, J = 29 Hz), −292.2 (1F, d, $^2J_{PF}$ = 120 Hz). $^{31}P\{^1H\}$ (121.5 MHz, C_6D_6) δ 61.4 (d, $^2J_{PF}$ = 120 Hz).

5.6. Catalytic activity of **1** and **5** in Suzuki type cross-coupling reactions

(a) In an NMR tube phenyl boronic acid (33 mg, 0.27 mmol) was added to a mixture of *trans*-[Ni(F)(2-C_5NF_4)(^{i}Pr$_2$PCH$_2$CH$_2$OMe)$_2$] (**1**) and *trans*-[Ni(F)(4-C_5NF_4)(^{i}Pr$_2$PCH$_2$CH$_2$OMe)$_2$] (**2**) (ratio 2:1; 5 mg, 0.009 mmol), pentafluoropyridine (10 μL, 0.18 mmol) and NEt_3 (36 μL, 0.26 mmol) in THF-d_8 (0.6 mL). The reaction mixture was then heated for 17 h to 60 °C. The yields of 3,4,5-trifluoro-2,6-diphenylpyridine **7** and 3,5-difluoro-2,4,6-triphenylpyridine **8** were determined on using an external standard of α,α,α-trifluorotoluene and are 20% (TON = 8) and 10% (TON = 6), respectively.

(b) In an NMR tube phenyl boronic acid (50 mg, 0.41 mmol) was added to a mixture of [Ni(F)(4-C_5NF_4){κ^2-(*P,N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**5**) and [Ni(F)(2-C_5NF_4){κ^2-(*P,N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**4**) (ratio 2:1; 5 mg, 0.014 mmol), pentafluoropyridine (15 μL, 0.14 mmol) and NEt_3 (56 μL, 0.41 mmol) in THF-d_8 (0.6 mL). The reaction mixture was then heated for 17 h to 60 °C. The yield of **8** was determined on using an external standard of α,α,α-trifluorotoluene and is 13% (TON = 8).

5.7. Catalytic formation of 3,5-difluoro-2,6-diphenylpyridine (**9**)

(a) In an NMR tube phenyl boronic acid (34 mg, 0.28 mmol) was added to a mixture of *trans*-[Ni(F)(2-C_5NHF_3)(^{i}Pr$_2$PCH$_2$CH$_2$OMe)$_2$] (**3**) (4 mg, 0.007 mmol), 2,3,5,6-tetrafluoropyridine (8 μL, 0.14 mmol) and Cs_2CO_3 (102 mg, 031 mmol) in THF-d_8 (0.6 mL). The reaction mixture was heated for 3 h to 60 °C. The yield of **9** was determined on using an external standard of fluorobenzene and is 99% (TON = 40).

(b) In an NMR tube phenyl boronic acid (46 mg, 0.38 mmol) was added to a solution of [Ni(F)(4-C_5NHF_3){κ^2-(*P,N*)-^{i}Pr$_2$*P*CH$_2$CH$_2$*N*Me$_2$}] (**6**) (5 mg, 0.013 mmol), 2,3,5,6-tetrafluoropyridine (13 μL, 0.13 mmol) and Cs_2CO_3 (122 mg, 0.38 mmol) in THF-d_8 (0.6 mL). The reaction mixture was heated for 3d to 60 °C. The yield of **9** was determined on using an external standard of α,α,α-trifluorotoluene and is 17% (TON = 7).

ESI-MS (**9**) calc. for $C_{17}H_{11}NF_2^+$: *m/z* 268.0932; found: 268.0938.

5.8. Catalytic formation of 3,5-difluoro-2,6-di(4-methylphenyl)pyridine (**10**)

In an NMR tube tolyl boronic acid (38 mg, 0.28 mmol) was added to a mixture of *trans*-[Ni(F)(2-C_5NHF_3)(^{i}Pr$_2$PCH$_2$CH$_2$OMe)$_2$] (**3**) (4 mg, 0.007 mmol), 2,3,5,6-tetrafluoropyridine (8 μL, 0.14 mmol) and Cs_2CO_3 (101 mg, 0.31 mmol) in THF-d_8 (0.6 mL). The reaction mixture was heated for 3 h to 60 °C. The yield of **11**

was determined on using an external standard of fluorobenzene and is 98% (TON = 39). ESI-MS calc. for $C_{19}H_{15}NF_2^+$: *m*/*z* 296.1251; found: 296.1239.

5.9. Catalytic formation of 3,5-difluoro-2,6-di(4-trifluormethylphenyl)pyridine (**11**)

In an NMR tube 4-trifluormethylphenyl boronic acid (53 mg, 0.28 mmol) was added to a mixture of *trans*-[Ni(F)(2-C_5NHF_3)(^{i}Pr$_2$PCH$_2$CH$_2$OMe)$_2$] (**3**) (4 mg, 0.007 mmol), 2,3,5,6-tetrafluoropyridine (8 μL, 0.14 mmol) and Cs_2CO_3 (97 mg, 0.30 mmol) in THF-d_8 (0.6 mL). The reaction mixture was heated for 3 h to 60 °C. The yield of **12** was determined on using an external standard of fluorobenzene and is 95% (TON = 38). ESI-MS calc. for $C_{19}H_9NF_8^+$: *m*/*z* 404.0686; found: 404.0679.

5.10. Catalytic formation of 3,5-difluoro-2,6-di(4-methoxyphenyl)-pyridine (**12**)

In an NMR tube 4-methoxyphenyl boronic acid (55 mg, 0.36 mmol) was added to a mixture of *trans*-[Ni(F)(2-C_5NHF_3)(^{i}Pr$_2$PCH$_2$CH$_2$OMe)$_2$] (**3**) (5 mg, 0.009 mmol), 2,3,5,6-tetrafluoropyridine (10 μL, 0.18 mmol) and Cs_2CO_3 (120 mg, 0.37 mmol) in THF-d_8 (0.6 mL). The reaction mixture was heated for 3 h to 60 °C. The yield of **13** was determined on using an external standard of fluorobenzene and is 97% (TON = 39). ESI-MS calc. for $C_{19}H_{15}NF_2O_2^+$: *m*/*z* 328.1149; found: 328.1148.

5.11. Structure determination for the complexes **3**, **5** and **6**

Yellow crystals of **3** were obtained from *n*-hexane at 0 °C. **5** and **6** were crystallized via gas phase diffusion of *n*-hexane in a THF solution. The diffraction data were collected on a STOE IPDS 2θ diffractometer at −173 °C. Crystallographic data are depicted in Table 7. The structures were solved by direct methods and refined with the full matrix least squares method on F^2 (SHELX-97).

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