FEATURE ARTICLE

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Routes to fluorinated organic derivatives by nickel mediated C–F activation of heteroaromatics

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New fluorinated azaheterocycles can be synthesised regio- and chemo-selectively *via* C–F activation of fluorinated precursors at nickel, with subsequent functionalisation and release from the coordination sphere of the metal; the requirements for productive C–F activation are significantly different from those for C–H bond activation.

Introduction

The introduction of fluorinated groups into organic molecules can cause a dramatic change in their physical properties, chemical reactivity and physiological activity. This is illustrated by the application of fluorinated pyrimidines or pyridines as liquid crystals, herbicides, insecticides, anti-cancer agents and antibiotics.[1] However, it is still a challenge for synthetic chemists to prepare the desired molecules. The typical synthetic routes to fluorinated azaheterocycles involve introduction of fluorine at key positions or functionalisation of the fluorinated aromatics *e.g.* by nucleophilic substitution of a fluorine.[1–3] Our strategy for the synthesis of a polyfluorinated aromatic molecule is totally different and is initiated by the selective replacement of a fluorine atom by a transition metal.[2] Once the aromatic ring is attached to the metal centre, the fluorinated organic ligand can then be derivatised to yield new fluoro-organic molecules.

Thomas Braun did his undergraduate and graduate studies at the University of Würzburg. He received his PhD under the supervision of H. Werner for his thesis on the synthesis and reactivity of ruthenium carbene complexes. After a short period at the University of Rennes with P. H. Dixneuf he moved to York in 1997, where he was a post-doctoral fellow with R. N. Perutz. In 2000 he joined the group of P. Jutzi at the Chemistry Department of the University of Bielefeld to finish his habilitation. His research interests range from fluorine chemistry to coordination and organometallic chemistry. The main research areas include the synthesis and reactivity of transition metal fluorides, the C–F activation of fluoro-organic molecules with transition metals and the functionalisation of fluorinated molecules in the coordination sphere of a metal.

Robin Perutz studied the structure of metal carbonyl fragments for his PhD under J. J. Turner. In that period in Cambridge and Newcastle, he established the existence of one of the first σ-complexes, $Cr(CO)_5(CH_4)$, and the first metal–Xe bond, $Cr(CO)_5Xe$, by photochemical matrix isolation. After periods in Mülheim, Edinburgh and Oxford, he moved to York in 1983 where he is now Head of Department. Along the route, he broadened his interest to encompass many aspects of the reaction mechanisms, photochemistry, spectroscopy and synthesis of organo-transition metal and metal hydride complexes. For instance, he has measured the rates of oxidative addition of H–H, C–H and Si–H bonds at 4-coordinate Ru(0) centres and shown that oxidative addition of dihydrogen may occur with essentially no activation barrier. Recently, he has turned his hand to supramolecular photochemistry. He has delivered the Tilden Lecture of the Royal Society of Chemistry, the Dow Lectures at the University of Ottawa and the Seaborg Lectures at the University of California, Berkeley.

C–F Activation reactions of fluorinated heterocycles at nickel and their mechanisms

Several methods have been reported for the activation of a carbon–fluorine bond at appropriate transition metal centres.[4] Some of the discoveries are summarised in thorough reviews.[4] One approach we have studied in the last few years is the fast oxidative addition of fluorinated heteroaromatics such as pentafluoropyridine, 2,3,4,5-tetrafluoropyridine, 2,3,5,6-tetrafluoropyridine or 2,4,6-trifluoropyrimidine at a nickel centre giving *trans*-[NiF(2-C_5NF_4)$(PEt_3)_2$] **1**, *trans*-[NiF(2-C_5NF_3H)$(PEt_3)_2$] **2**, **3** and *trans*-[NiF(4-$C_4N_2F_2H$)$(PEt_3)_2$] **4** in high yield (Scheme 1).†[5–7] The reactions are carried out in a non-polar solvent, typically hexane, at room temperature. The intermolecular reactions are regioselective and chemospecific for C–F over C–H activation. The specificity is particularly striking in the reaction to form **3** (Scheme 1). The reactions also proceed far more rapidly than the analogous activation of hexafluorobenzene yielding *trans*-[NiF(C_6F_5)$(PEt_3)_2$] **5**.[5,8] The role of the nitrogen atom in the heterocycles in accelerating the reactions is not fully understood.

Complexes **1**–**4** are representative of the class of nickel (aryl) fluoride complexes, that were unknown prior to our work. The X-ray structures of **2** and **4** show that nickel is square planar with the aryl group perpendicular to the coordination plane of nickel. The nickel–fluorine bond length is *ca.* 1.86 Å, close to expectations from well-known Ni–O bond lengths. The nickel–C(aryl) bond length is almost identical in length to the Ni–F bond. The most important solution characteristic is the fluoride ^{19}F NMR resonance that lies at high field, *ca.* δ −370, and is coupled to the ^{31}P nuclei (*ca.* 47 Hz) and the ^{19}F nuclei (*ca.* 9 Hz) on the aryl carbon atoms *ortho* to nickel.

Before considering the mechanism of reaction of the fluorinated heterocycles, we discuss the corresponding reactions of hexafluorobenzene and octafluoronaphthalene. There is strong evidence that precoordination of the aromatic compounds at the nickel centre is a crucial step in the activation of a C–F bond in fluorinated aromatic systems. This is indicated by the observed coordination and intramolecular activation of octafluoronaphthalene at {Ni$(PEt_3)_2$} yielding *trans*-[NiF(2-

† Pyridines are numbered with N in position 1, pyrimidines with N in positions 1 and 3.

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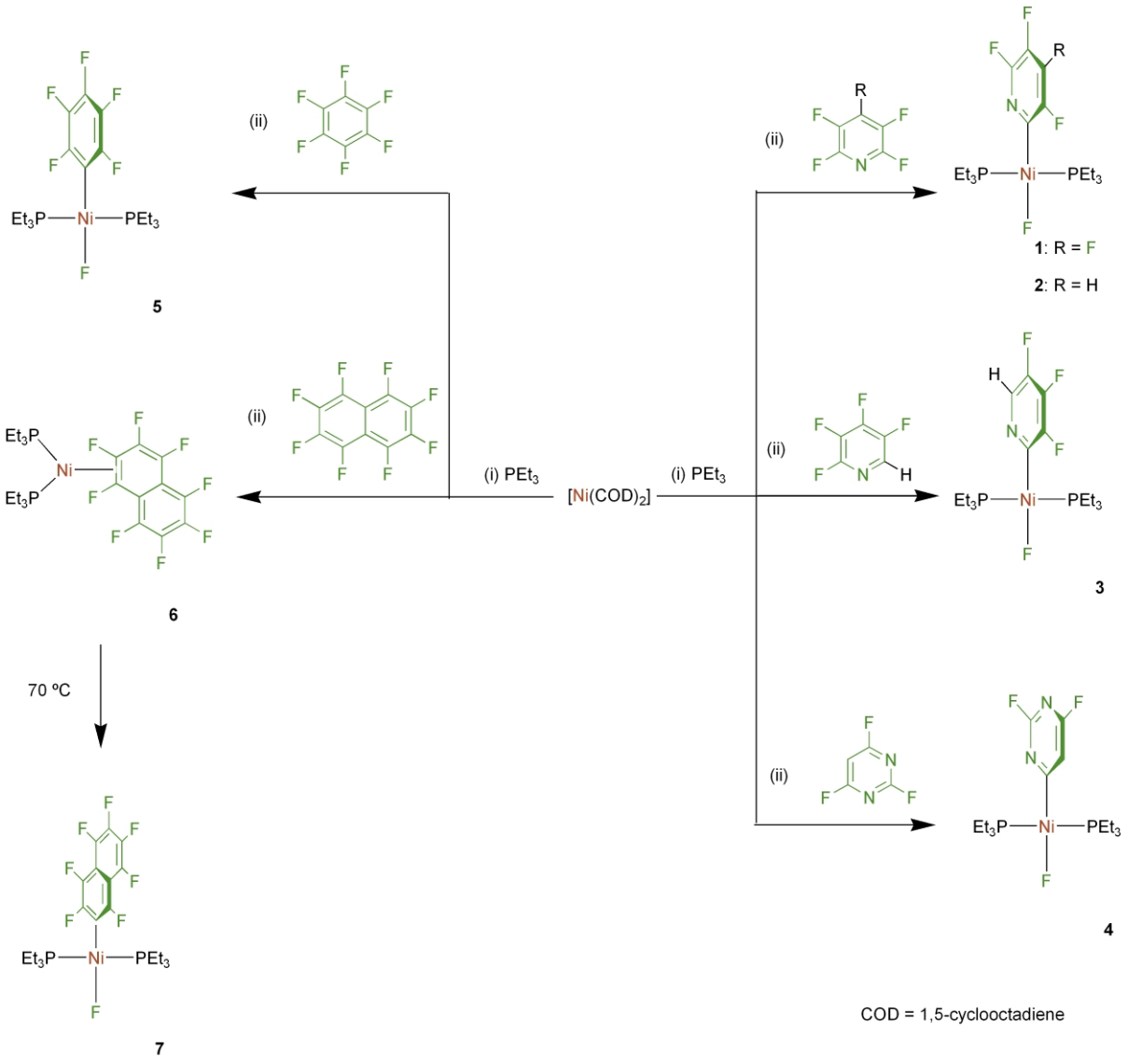
$C_{10}F_7)(PEt_3)_2]$ **7** (Scheme 1).[9] The crystal structure of the intermediate $[Ni(\eta^2\text{-}1,2\text{-}C_{10}F_8)PEt_3)_2]$ **6** shows asymmetric η^2-coordination of the aromatic system at nickel. The C–F bonds of the coordinated carbon atoms are extended and lie out of the octafluoronaphthalene plane. In addition, the Ni–C(2) is appreciably shorter than the Ni–C(1) bond (1.899(4) and 1.959(4) Å respectively, Fig. 1). Moreover, the rates of loss of **6** and formation of **7** are compatible with a concerted intramolecular oxidative addition of the octafluoronaphthalene ligand forming the Ni(II) C–F activation product **7**. Although the structure suggests an incipient transition state for concerted C–F activation, DFT calculations indicate that the potential for distortion of the coordination geometry is very soft. It should be mentioned that Crespo *et al.* have obtained kinetic evidence for a concerted oxidative addition of fluoroaromatic substituents in imines at platinum.[10] The hexafluorobenzene compound $[Ni(\eta^2\text{-}C_6F_6)\{t\text{Bu}_2\text{P}(CH_2)_2\text{P}t\text{Bu}_2\}]$ has also been synthesised and it has been shown that on heating it reacts to form $[NiF(C_6F_5)\{t\text{Bu}_2\text{P}(CH_2)_2\text{P}t\text{Bu}_2\}]$, but no kinetics are reported.[11]

Tsou and Kochi studied the reactions of $[Ni(PEt_3)_4]$ with Ar–X (X = I, Br, Cl) and showed that there are two competing pathways leading to $[Ni^{II}(PEt_3)_2(Ar)X]$ and $[Ni^{I}(PEt_3)_3X]$ + ArH, respectively.[12] The second pathway is of major importance when X = I, contributes < 10% of product when X = Br, and is not observed for X = Cl. Tsou and Kochi postulated that a tight ion-pair $\{Ni(PEt_3)_3^+ \cdot ArX^-\}$ precedes both products on the basis of solvent effects, substituents effects and deliberate addition of Ni(I).[12] In our reactions with fluoroaromatics, there is direct evidence for a $[Ni(PEt_3)_2(\eta^2\text{-arene})]$ intermediate, but we cannot exclude involvement of an ion pair in addition. There is no evidence for Ni^I products at all. We note that $C_6F_6^-$ would be short-lived since this species dissociates fluoride in solution leading to $C_6F_5\cdot$.[13] Theoretical studies of the reaction of $\{Ni(PH_3)_2\}$ with hexafluorobenzene show that product formation becomes increasing energetically favourable in the order $[Ni(PH_3)_2(\eta^2\text{-}C_6F_6)]$ < *cis*-$[Ni(PH_3)_2(C_6F_5)F]$ < *trans*-$[Ni(PH_3)_2(C_6F_5)F]$.[14] In contrast to C–F oxidative addition, the corresponding reaction of benzene to form *trans*-$[Ni(PH_3)_2(C_6H_5)H]$ is conspicuously unfavourable. The activation energy for conversion of $[Ni(PH_3)_2(\eta^2\text{-}C_6F_6)]$ to *cis*-$[Ni(PH_3)_2(C_6F_5)F]$ is calculated to be 97 kJ mol^{-1}.[14]

The reactions of fluoropyridines with $[Ni(COD)_2]$ proceed rapidly in a non-polar solvent with two equivalents of triethylphosphine and a slight excess of fluoropyridine, but no intermediates have been observed. The heteroaromatic systems may undergo C–F activation *via* η^2-coordination of the aromatic system or *via* nitrogen coordination. The former coordination mode has been observed in $[(\eta^5\text{-}C_5H_5)Rh(PMe_3)(\eta^2\text{-}C_5F_5N)]$, while the latter was reported by Bercaw *et al.* in the cationic



Scheme 1 C–F activation of fluorinated aromatics and heteroaromatics at nickel.

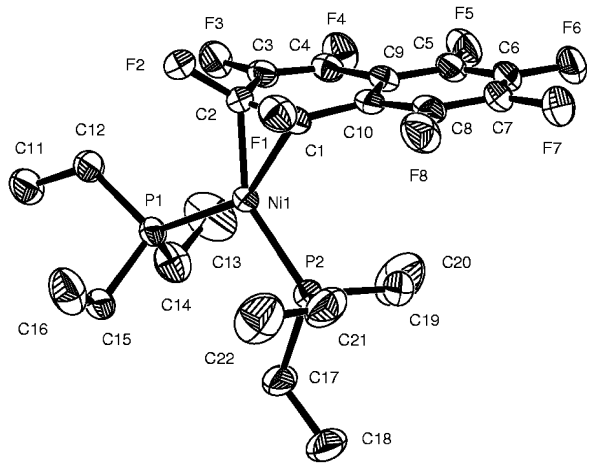
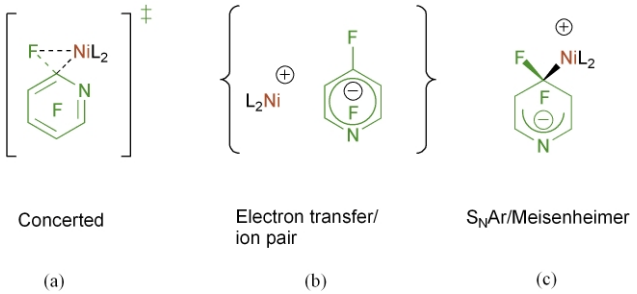


Fig. 1 An ORTEP diagram of **6**. Ellipsoids are drawn at the 50% probability level.

complex [(tmeda)Pt(CH_3)(NC_5F_5)]BAr′$_4$ [Ar′ = 3,5-$C_6H_3(CF_3)_2$].[15,16] Density functional calculations on coordination modes of pentafluoropyridine at {Ni(PH_3)$_2$} indicate that η^2-coordination *via* an aromatic C=C bond is preferred in this case.[14]

The observed preference for C–F activation at the 2-position of pentafluoropyridine provides indirect evidence for concerted oxidative addition of the azaheterocycles *via* a three-centred transition state [Scheme 2(a)]. An alternative electron transfer



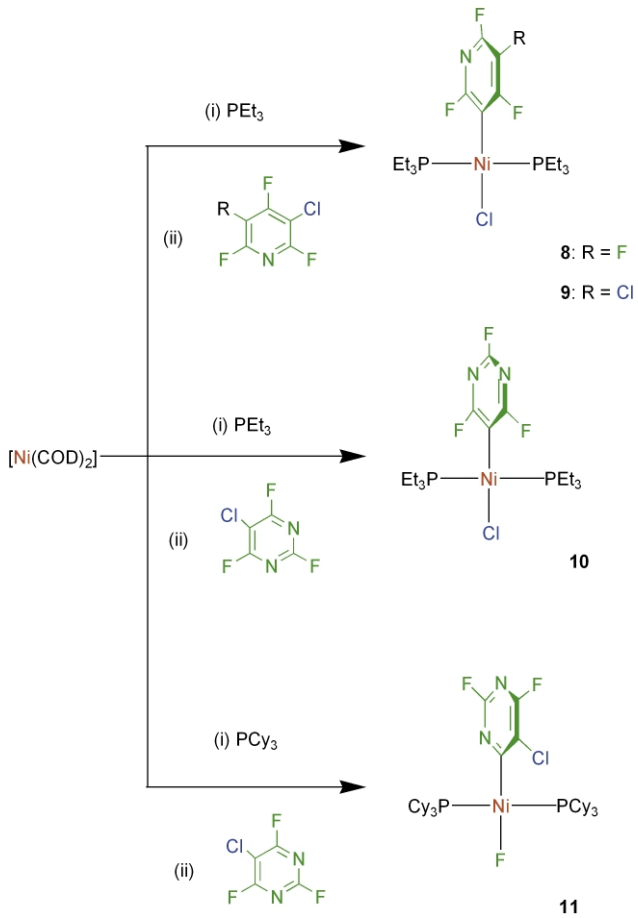
Scheme 2 Possible intermediates and transition state for the C–F activation of pentafluoropyridine at nickel.

reaction pathway *via* a tight ion pair [Scheme 2(b)] would lead to a reaction in the 4-position as has been established for other such reactions.[3] A S$_N$Ar type nucleophilic mechanism *via* a Meisenheimer intermediate [Scheme 2(c)] would probably also result in an attack at the 4-position of pentafluoropyridine as has been observed in countless reactions.[3] Exceptionally, the nucleophilic attack of the phosphine P*H*t*Bu*$_2$ at pentafluoropyridine takes place at the 2-position.[17] This regioselectivity has been explained by increased steric hindrance, but bulky anionic transition metal complexes such as [Co(CO)$_2$(PPh$_3$)$_2$]$^-$ or [Rh(CO)$_2$(PPh$_3$)$_2$]$^-$ react at the conventional 4-position of the heterocycle.[18]

Further evidence for a concerted pathway for the reaction of azaheterocycles at nickel is derived from competition experiments. They show that the nickel system reacts 4.5 times faster with pentafluoropyridine than with 2,4,6-trifluoropyrimidine, yet the pyrimidine undergoes nucleophilic attack thousands of times faster than the pyridine.[19] Thus, we have strong evidence for a concerted oxidative addition, although nucleophilic attack of the nickel centre at the heterocycle remains a possibility which we cannot exclude entirely.

Chemoselectivity of C–F activation reactions

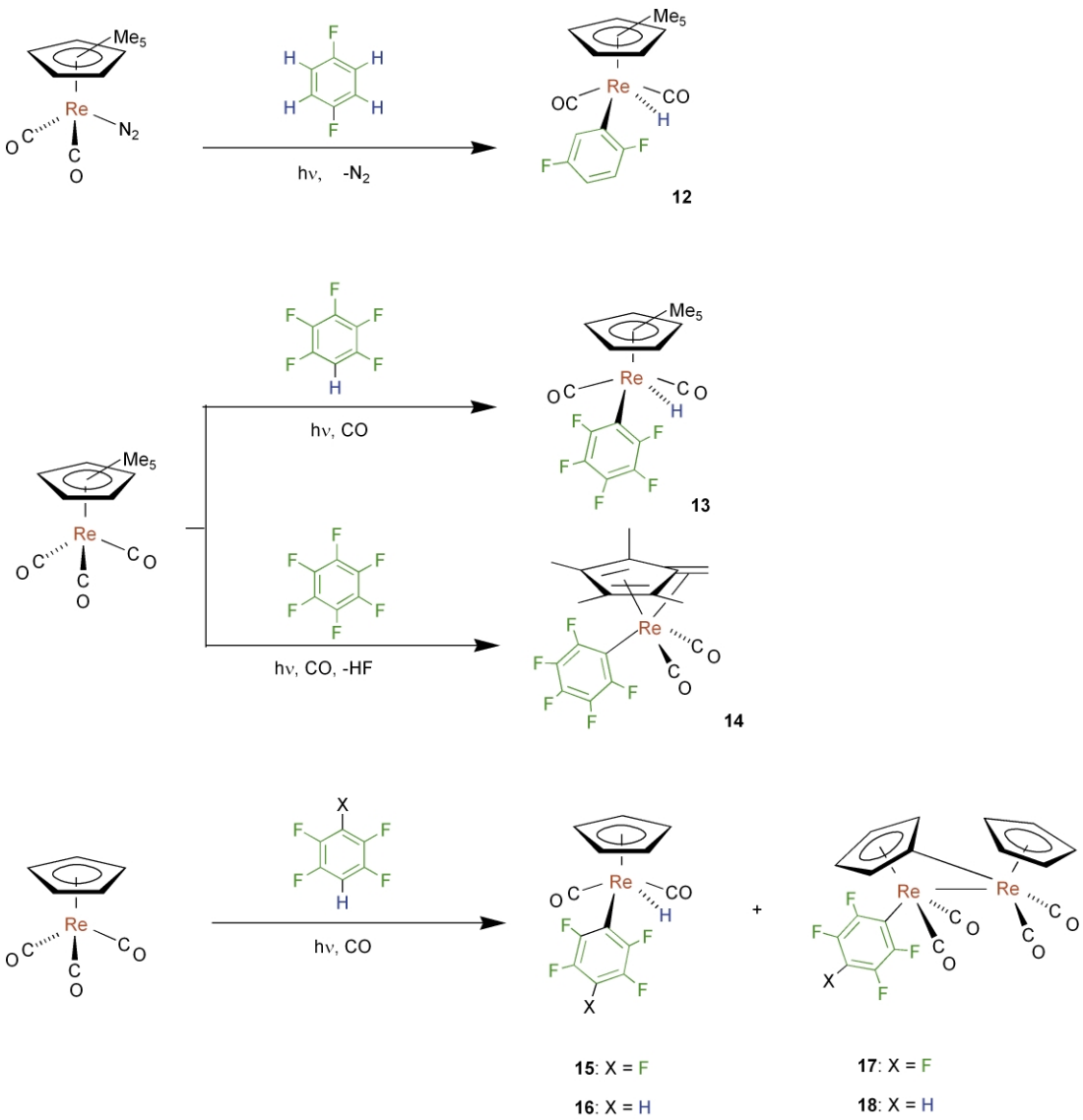
Fluorinated heterocycles also bearing a chlorine atom generally undergo C–Cl activation at {Ni(PEt_3)$_2$}. This has been demonstrated by the insertion of nickel in a C–Cl bond in 3-chlorotetrafluoropyridine, 3,5-dichlorotrifluoropyridine and 5-chloro-2,4,6-trifluoropyrimidine (Scheme 3).[5,20,21] However,



Scheme 3 Activation of azaheterocycles bearing a chlorine atom.

the activation of a C–F bond in the presence of a much weaker C–Cl bond in 5-chloro-2,4,6-trifluoropyrimidine can be accomplished using the sterically more hindered tricyclohexylphosphine yielding *trans*-[NiF(4-$C_4N_2ClF_2$)(PCy_3)$_2$] **11** together with a minor product (18%), which was assigned as *trans*-[NiCl(4-$C_4N_2ClF_2$)(PCy_3)$_2$].[21] Such an activation of a C–F bond in the presence of a C–Cl bond in the same ring has never been observed before. For comparison, Crespo *et al.* reported the C–F activation of the imine (C_6F_5)CH=NCH_2(2-ClC_6H_4) at a Pt(II) centre, but with the C–F and C–Cl bonds on different rings.[22]

Preference for C–F bond activation over C–H bond activation is critical to the development of applications since tolerance of C–H bonds is essential. As demonstrated by the DFT calculations, the reactions at {Ni(PH_3)$_2$} are energetically unfavourable for C–H bond activation but kinetically and energetically favourable for C–F bond activation.[14] The observed preference for C–F activation over C–H activation at nickel contrasts with observations at a rhenium centre, {(η^5-C_5Me_5)Re(CO)$_2$}. For instance, photochemical reaction of [(η^5-C_5Me_5)Re(CO)$_2$(N_2)] with 1,4-difluorobenzene yields the C–H activation product [(η^5-C_5Me_5)Re(H)($C_6H_3F_2$)(CO)$_2$] **12** (Scheme 4).[23] Comparable results are obtained with the more fluorinated benzenes C_6HF_5 and 1,2,4,5-$C_6H_2F_4$. Thus, UV irradiation of [(η^5-C_5Me_5)Re(CO)$_3$] in the presence of C_6HF_5 affords [(η^5-C_5Me_5)Re(H)(C_6F_5)(CO)$_2$] **13** as the principal product.[24] However, it is C–F activation in combination with intramolecular C–H activation that dominates on photolysis of [(η^5-



Scheme 4 C–F and C–H activation reactions at rhenium.

$C_5Me_5)Re(CO)_3]$ in neat C_6F_6 yielding the tetramethylfulvene complex $[(\eta^6\text{-}C_5Me_4CH_2)Re(C_6F_5)(CO)_2]$ **14**.[25] The C–H activation products **15** and **16** are generated with the cyclopentadienyl analogue $[(\eta^5\text{-}C_5H_5)Re(CO)_3]$ and C_6HF_5 or $C_6H_2F_4$. There are minor by-products including bis(aryl) complexes produced by C–F activation of a second aromatic molecule as well as the binuclear complexes **17** and **18**.

Other transformations with a preference for C–H activation over C–F activation have been described at rhodium.[26,27] While the complex $[(\eta^5\text{-}C_5Me_5)Rh(PMe_3)(C_2H_4)]$ and C_6F_6 can be converted to the fluoro complex $[(\eta^5\text{-}C_5Me_5)Rh(F)(C_6F_5)(PMe_3)]$ by photochemical means in liquid hexafluobenzene, the thermal reaction of 1,4-difluorobenzene with $[(\eta^5\text{-}C_5Me_5)Rh(H)(Ph)(PMe_3)]$ gives the C–H activation product $[(\eta^5\text{-}C_5Me_5)Rh(H)(C_6F_2H_3)(PMe_3)]$. The cyclopentadienyl complex $[(\eta^5\text{-}C_5H_5)Rh(PMe_3)(C_2H_4)]$ shows a preference for C–H activation too reacting photochemically with 1,4-difluorobenzene to form $[(\eta^5\text{-}C_5H_5)Rh(H)(C_6F_2H_3)(PMe_3)]$. Density functional calculations for the oxidative addition of 1,4-difluorobenzene at $[(\eta^5\text{-}C_5H_5)Rh(\eta^2\text{-}C_6F_2H_4)(PH_3)]$ show that both C–F and C–H bond activation are energetically favourable (contrast nickel). They support a mechanism with concerted oxidative addition to the 16-electron fragment $\{(\eta^5\text{-}C_5H_5)Rh(PH_3)\}$ and show that the preference for C–H activation is of kinetic origin.[27]

Preference for C–F over C–H bond activation can be achieved by reaction of some dihydride complexes with fluorobenzenes. *cis*-$[RuH_2(dmpe)_2]$ yields products of C–F bond activation with pentafluorobenzene, tetrafluorobenzenes or 1,2,3-trifluorobenzene.[13] The reaction is unaffected by added fluoride. As postulated for other transformations at rhodium or iridium, this reaction is thought to proceed by an electron transfer mechanism rather than by a simple oxidative addition.[4,28–30] A base-catalysed mechanism has been postulated by W. D. Jones *et al.* in the C–F bond activation of fluorinated benzenes using $[(\eta^5\text{-}C_5Me_5)Rh(H)_2(PMe_3)]$ as substrate.[31] This nucleophilic mechanism includes an attack of $[(\eta^5\text{-}C_5Me_5)Rh(H)(PMe_3)]^-$ at C_6F_5H and explains the observed preference for C–F over C–H activation. These reactions are less suited to formation of new organic products than the reactions at nickel because of the *trans*-octahedral structure of the ruthenium products and the difficulty of reductive elimination at $\{(\eta^5\text{-}C_5Me_5)Rh(PMe_3)\}$.

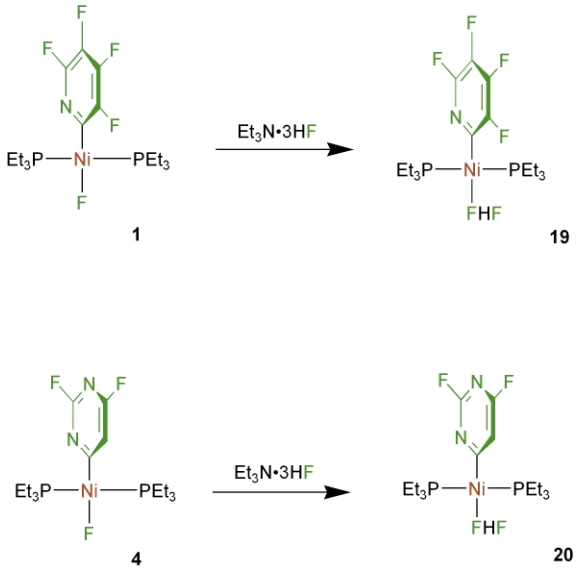
Reactivity of nickel fluorides

Transition metal complexes bearing a fluoro ligand are increasingly regarded as valuable compounds in organometallic chemistry with interesting properties as catalysts or synthetic

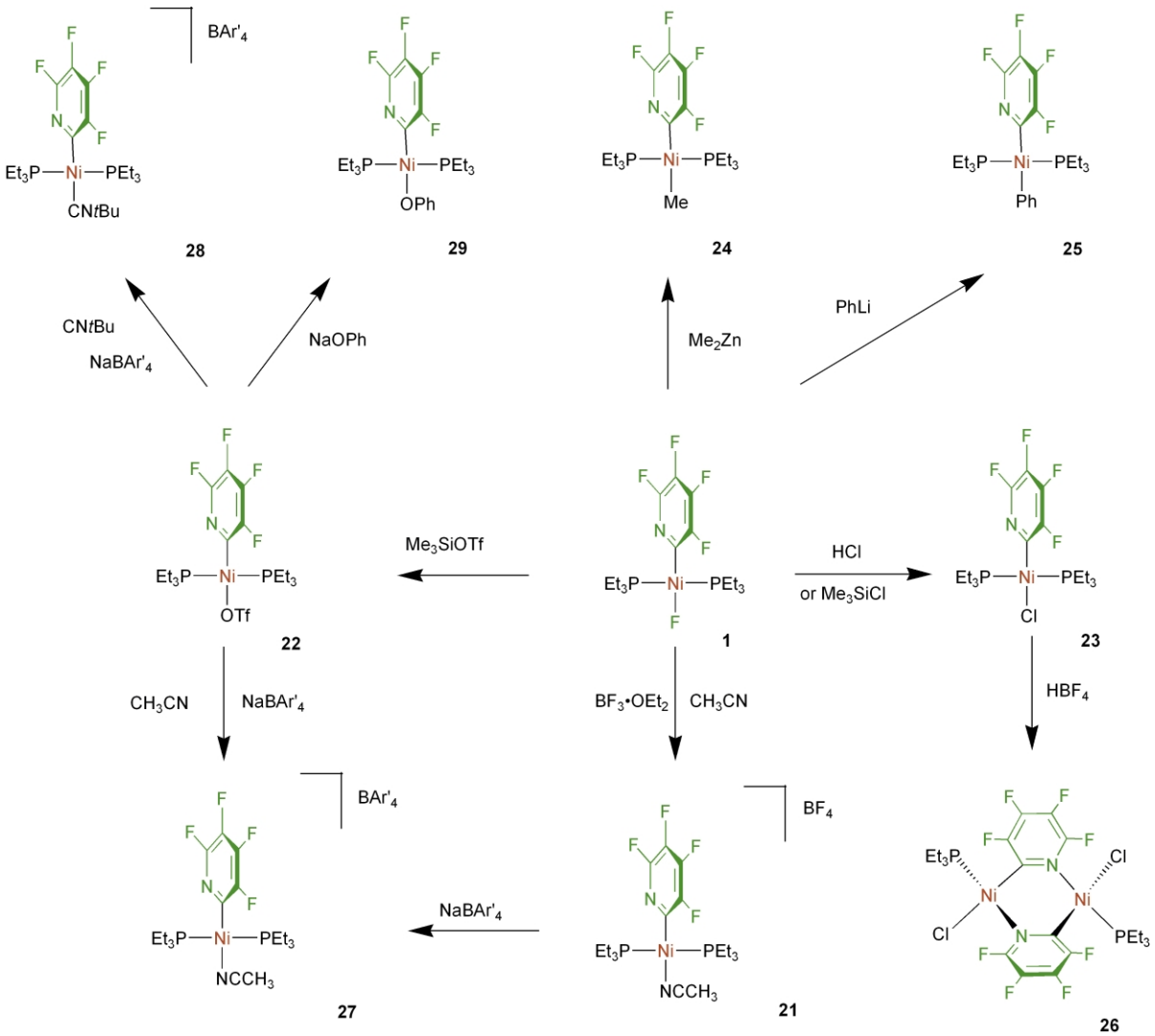
precursors.[4,32] One other special feature of metal–fluoride complexes is that they are capable of coordinating hydrogen fluoride *via* hydrogen bonds, thus forming coordinated bifluoride (FHF).[6,7,33] The bifluoride complexes *trans*-[Ni(FHF)(2-C_5NF_4)(PEt_3)$_2$] **19** and *trans*-[Ni(FHF)(4-$C_4N_2F_2H$)(PEt_3)$_2$] **20** have been prepared by reaction of $Et_3N{\cdot}3HF$ with nickel fluorides and characterised in solution (Scheme 5).[6,7] An X-ray structural analysis of **20** suggests that the FHF interaction is best described as a hydrogen bond between a NiF moiety and HF.[6] The Ni–F bond length is 1.908(3) Å compared to 1.856(2) Å for *trans*-[NiF(2-C_5NF_3H)(PEt_3)$_2$] **2** indicating that the hydrogen bonding causes some lengthening of the Ni–F bond.

The reactivity of nickel fluoride compounds bearing polyfluoropyridyl ligands has also been investigated.[7] Fluoride may be abstracted with BF_3 or with Me_3Si derivatives. Thus, treatment of **1** with $BF_3{\cdot}OEt_2$ in the presence of acetonitrile yields the cationic compound *trans*-[Ni(2-C_5NF_4)(NCMe-)(PEt_3)$_2$]BF_4 **21**. [Ni(OTf)(2-C_5NF_4)(PEt_3)$_2$] **22** can readily be synthesised from **1** and Me_3SiOTf.[34] Similarly, the chloride **23** can be formed by reaction of **1** with Me_3SiCl. The reaction of **1** with HCl provides an alternative route to **23** (Scheme 6).[7]

Although free tetrafluoropyridine reacts rapidly with nucleophiles, the nickel complexes react with nucleophiles at the metal resulting in replacement of the fluoride.[3] Thus, we have successfully replaced Ni–F in *trans*-[NiF(2-C_5NF_4)(PEt_3)$_2$] **1** by Ni–C bonds by reaction with Me_2Zn or PhLi yielding *trans*-[NiMe(2-C_5NF_4)(PEt_3)$_2$] **24** and *trans*-[NiPh(2-C_5NF_4)(PEt_3)$_2$] **25** (Scheme 6).[34] Some of these reactions can be used in the synthesis of new non-metallated heterocycles as described below.



Scheme 5 Formation of nickel bifluorides.



Scheme 6 Reactivity of **1**.

The chloride and triflate derivatives are useful precursors in their own right. Treatment of *trans*-[NiCl(2-C_5NF_4)(PEt_3)$_2$] **23** with HBF_4 abstracts PEt_3 to afford the binuclear complex [NiCl{μ-κ^2(*C*,*N*)-(2-C_5NF_4)}(PEt_3)]$_2$ **26**.[7] The X-ray crystal structure of **26** reveals a 'butterfly'-shaped dimeric complex with square-planar coordination at both nickel atoms (Scheme 6, Fig. 2). Reaction of *trans*-[Ni(OTf)(2-C_5NF_4)(PEt_3)$_2$] **22**

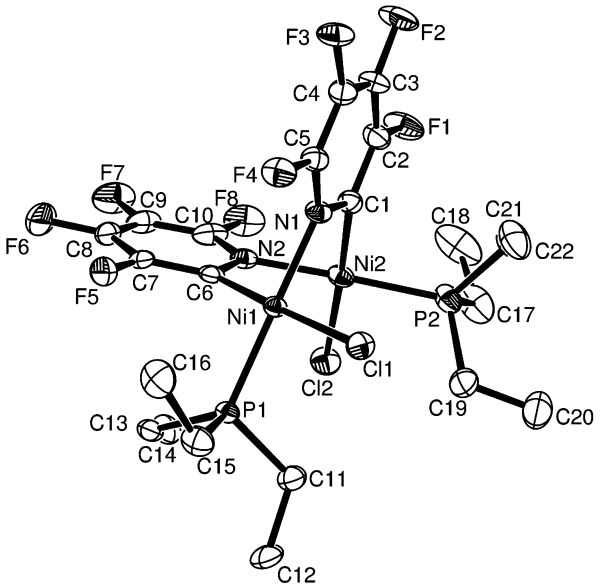


Fig. 2 An ORTEP diagram of **26**. Ellipsoids are drawn at the 50% probability level.

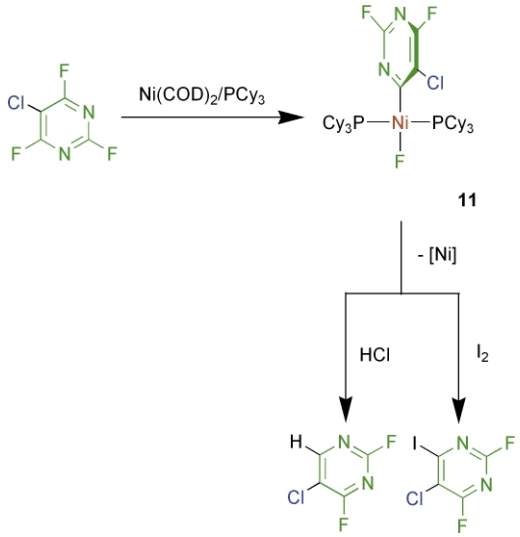
with $NaBAr'_4$ [Ar′ = 3,5-$C_6H_3(CF_3)_2$] and acetonitrile or CN*t*Bu gives *trans*-[Ni(2-C_5NF_4)(NCMe)(PEt_3)$_2$]BAr'_4 **27** and *trans*-[Ni(2-C_5NF_4)(CN*t*Bu)(PEt_3)$_2$]BAr'_4 **28**.[7,35] The triflate complex **22** can also be converted into the phenoxy compound *trans*-[Ni(OPh)(2-C_5NF_4)(PEt_3)$_2$] **29** on treatment with NaOPh.

Nickel-mediated synthesis of new heterocycles

The reactions of fluorinated precursors at nickel provide access to fluorinated heterocycles, which are otherwise inaccessible. Overall, we start with a commercially available fluorinated heterocycle, selectively remove a fluorine from it by reaction at nickel, and then functionalise further. The unusual substitution patterns in the final product arise from the initial chemo- and regioselective attack by nickel.[2] Note that no tetrafluoropyridyl complexes with the metal in the 2-position had been described previously.[34] The new heterocycles can usually be obtained in an overall yield of 20–50% based on the organo-fluoro starting compound.

This strategy is demonstrated by the activation of pentafluoropyridine in the 2-position followed by the sequential methylation of *trans*-[NiF(2-C_5NF_4)(PEt_3)$_2$] **1** and reaction with CO, which affords the ketone 2-C_5F_4NC(=O)Me by elimination (Scheme 7).[34] It is normally very difficult to prepare tetrafluoropyridines substituted in the 2-position.[2,3] Complex **1** can be used to synthesise a variety of these compounds: for instance, reaction of **1** with iodine affords 2-C_5F_4NI, while prolonged treatment of **1** with HCl gives 2-C_5F_4NH.[2,7] On admission of air to a solution of the methyl complex *trans*-[NiMe(2-C_5NF_4)(PEt_3)$_2$] **24**, the reductive elimination product 2-C_5F_4NMe is formed.[34]

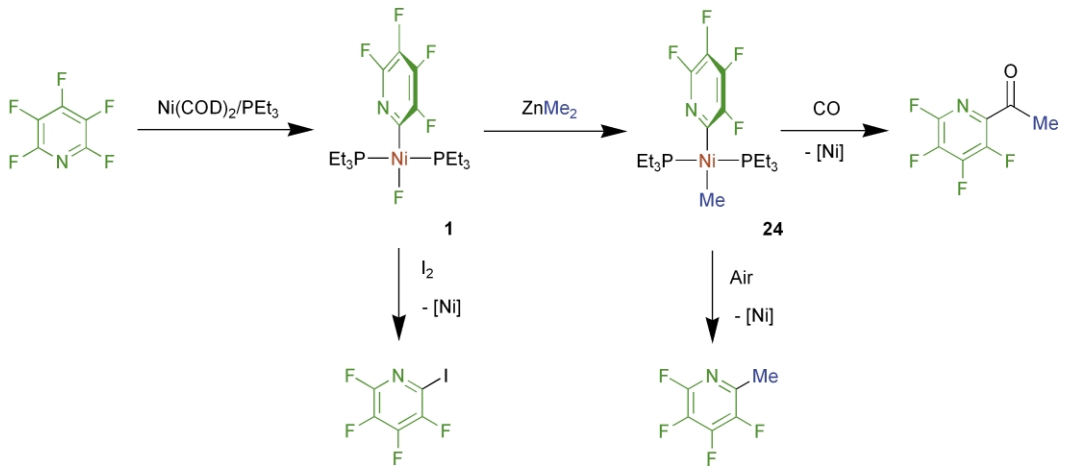
The nickel-mediated approach provides an unusual entry to halopyrimidines bearing three different substituents by removal of a fluorine from 5-chlorotrifluoropyrimidine (Scheme 8).[21]



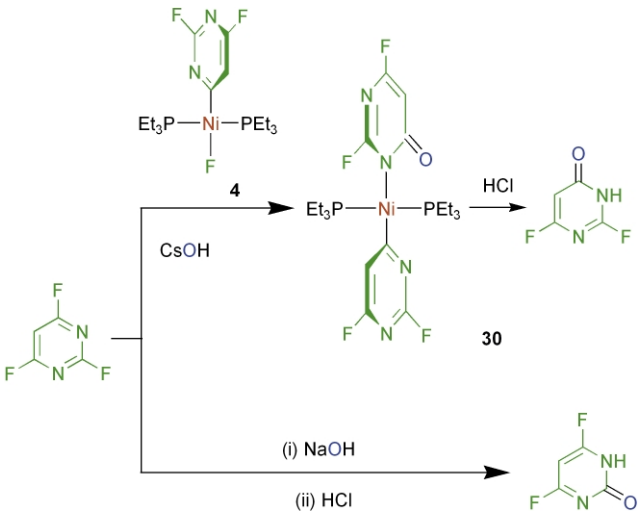
Scheme 8 Nickel-mediated derivatisation of 5-chlorotrifluoropyrimidine.

Treatment of *trans*-[NiF(4-$C_4N_2ClF_2$)(PCy_3)$_2$] **11** with HCl or iodine affords 5-chloro-2,4-difluoropyrimidine and 5-chloro-2,6-difluoro-4-iodopyrimidine.

In another intriguing example, the metal-mediated C–F activation of 2,4,6-trifluoropyrimidine again has the attraction of producing different regiochemistry from the typical organic route (Scheme 9).[6] Treatment of *trans*-[NiF(4-$C_4N_2F_2H$)(PEt_3)$_2$] **4** with CsOH in the presence of 2,4,6-tri-



Scheme 7 Nickel-mediated derivatisation of pentafluoropyridine.



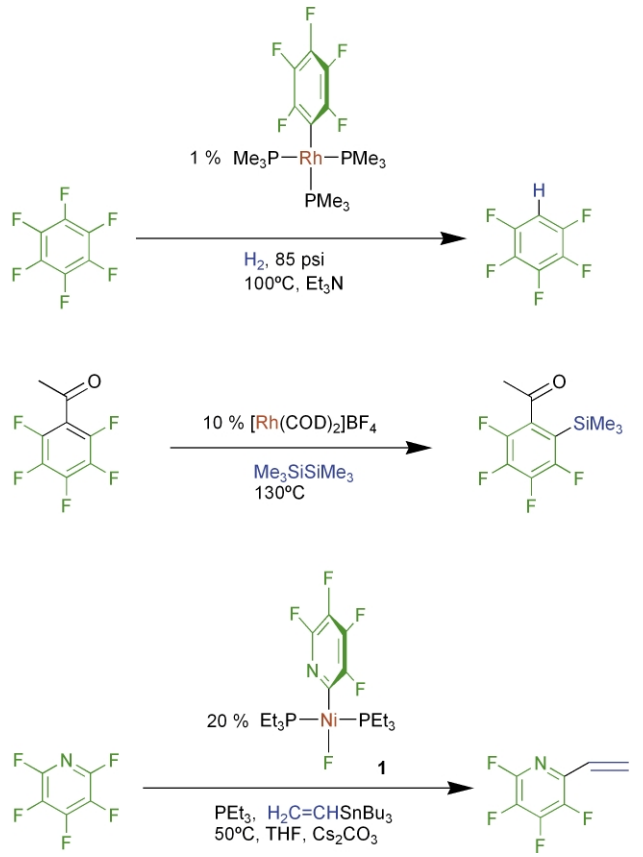
Scheme 9 Synthesis of fluorinated pyrimidinones.

fluoropyrimidine affords a nickel derivative of a pyrimidin-4-one **30** with the heterocyclic unit bound as an anionic ligand *via* a nitrogen atom at the metal. On treatment of **30** with HCl the free difluoropyrimidin-4-one can be obtained. Note that the reaction of 2,4,6-trifluoropyrimidine with NaOH results in the formation of the difluoropyrimidin-2-one.

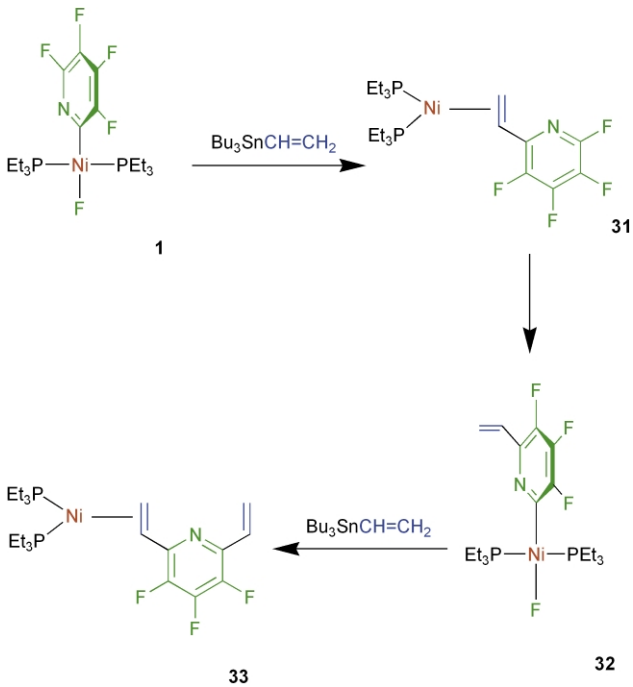
Catalytic conversions by C–F activation at nickel

Catalytic C–F activation of polyfluoroaromatics has become a reality, but the examples are sparse and have been limited to the formation of new C–H or C–Si bonds.[28,29,36] Milstein observed the catalytic conversion of hexafluorobenzene to pentafluorobenzene (Scheme 10) using hydrogen and [HRh(PMe$_3$)$_4$] as catalyst.[29] Murai and coworkers reported the rhodium-mediated silylation of pentafluoroacetophenone.[36] Other research groups demonstrated catalytic conversions of monofluorinated aromatics forming new C–H or C–C bonds.[37,38]

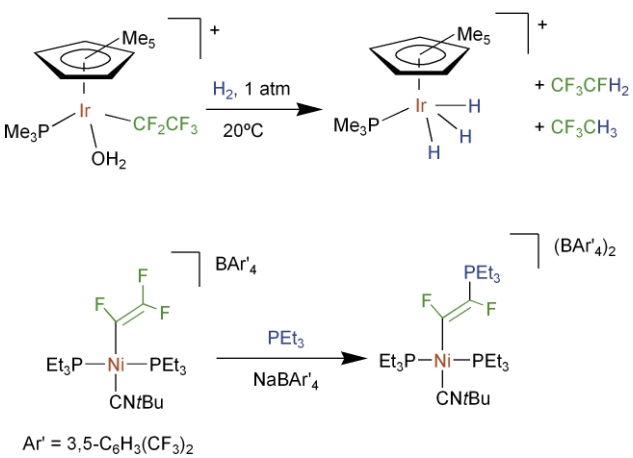
We achieved the catalytic conversion of pentafluoropyridine and 2,3,5,6-tetrafluoropyridine to their 2-vinyl derivatives by cross-coupling reactions with H_2C=CHSnBu$_3$ using a nickel catalyst (Scheme 10).[39] They represent the first catalytic C–C coupling reactions involving C–F activation of a polyfluorinated molecule. We also found that the cross-coupling reactions are likely to proceed *via* the formation of the η^2-vinylpyridine complex [Ni{η^2-2-C_5NF_4(CH=CH$_2$)}(PEt$_3$)$_2$] **31**, which was observed during the stoichiometric reaction of *trans*-[NiF(2-C_5NF_4)(PEt$_3$)$_2$] **1** with H_2C=CHSnBu$_3$ (Scheme 11). However, **31** is not stable in solution and two further compounds are observed after 1 d of reaction. They were assigned as the C–F activation product **32** and the divinylpyridine complex [Ni{η^2-2,6-C_5NF_3(CH=CH$_2$)$_2$}(PEt$_3$)$_2$] **33**. At present, the catalytic reactions are limited to a few turnovers, possibly because of competing decomposition pathways during the oxidative addition under catalytic conditions.[40]



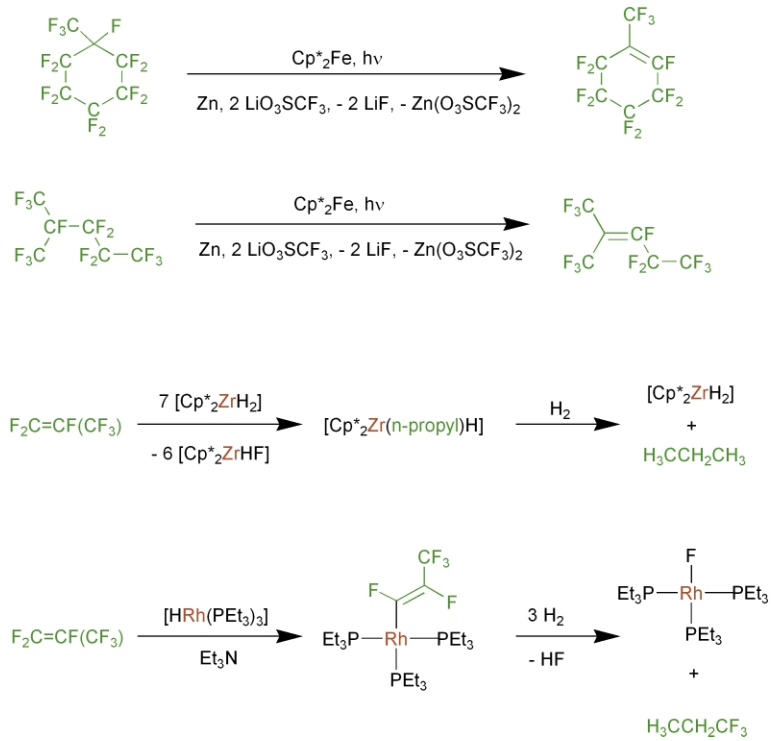
Scheme 10 Catalytic conversions of fluorinated aromatics by C–F activation (see refs 29, 36 and 39).



Scheme 11 Reaction of **1** with $Bu_3SnCH=CH_2$.



Scheme 12 Reactivity of fluorinated ligands (see refs 41–43).



Scheme 13 Metal-mediated derivatisation of perfluorinated alkenes and alkanes (see refs 44–47).

Outlook

Future goals in the area of C–F activation at transition metals still involve the development of new fluorinated building blocks, which are not accessible by current technology. To find catalytic transformations with high turnover numbers will certainly be one of the major challenges. One of the next stages is to synthesise some compounds with biological activity *via* metal-mediated selective removal of fluorine from polyfluorinated precursors.[1]

The special properties of anionic fluorocarbon ligands bound to a transition metal centre will lead to new and unexpected reaction pathways. For instance, Hughes *et al.* have already demonstrated that fluorinated alkyl ligands at iridium can be hydrogenated (Scheme 12).[41,42] Another example is represented by the nucleophilic substitution of a fluorine atom by a phosphine in a perfluorovinyl ligand at a cationic nickel complex (Scheme 12).[43]

One other demanding goal is the activation and selective functionalisation of fluorinated alkenes or even alkanes in the coordination sphere of a metal. The heterogeneous, catalytic conversion of fluorinated alkanes and cycloalkanes to alkenic and aromatic compounds has already been documented by the research groups of Richmond and Crabtree (Scheme 13).[4,44] The homogeneous reduction of hexafluoropropene to propane or 1,1,1-trifluoropropane has been achieved recently using zirconium or rhodium complexes (Scheme 13).[45,46] The zirconium-mediated conversion of 1-fluorohexane into hexane has also been reported.[45,47] These examples show that the activation and functionalisation of fluorinated olefins and alkanes in the coordination sphere of a metal certainly holds out promise of further surprising and exciting results in the near future.

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