C–F Bond Activation

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Selective C–F Bond Activation of Tetrafluorobenzenes by Nickel(0) with a Nitrogen Donor Analogous to N-Heterocyclic Carbenes**

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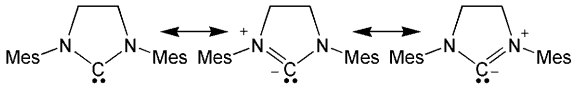
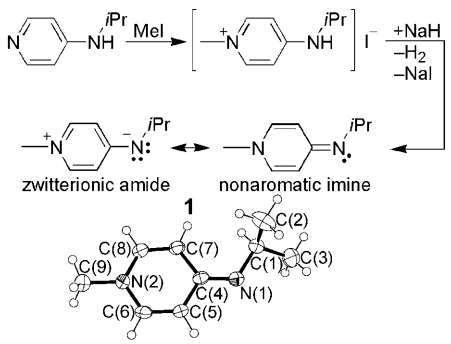
N-heterocyclic carbenes (NHCs) have gained recent prominence as alternatives to the ubiquitous phosphine donors as ancillary ligands for both stoichiometric and catalytic transformations.[1–5] The strong σ-donor abilities[6] of this class of ligands have a profound effect on reactivity; for example, the use of these donors often permits the oxidative addition of substrates that are otherwise unreactive.[7] Although these donors are commonly described as predominantly carbene-like in character, ylid resonance structures with carbanion character may also be drawn (Scheme 1).



Scheme 1. Carbene Structure **A** and zwitterionic resonance structures **B**. Mes = 2,4,6-$Me_3C_6H_2$

We sought to modify nitrogen donors using a similar strategy. Amido donors (R_2N^-) are well known to stabilize high-oxidation-state early-transition-metal complexes by virtue of the fact that they are hard donors capable of both σ and π donation.[8] These donors should be ideal for promoting oxidative addition reactions with the late transition metals. However, the excessively hard donor properties of amido ligands and the strongly π-antibonding interactions between the occupied metal d orbitals and the nitrogen-based lone pair often renders these donors too reactive for use as ancillary ligands with these low-valent soft metals.[9–13] The anionic charge of amido donors also impedes the utility of these donors in catalysis; the low oxidation state of the majority of active species in late-transition-metal catalysis mandates the use of neutral ancillary ligands to maintain sufficient reactive sites. A nitrogen-donor ligand with amido-donor-like properties but a net neutral charge and diminished π-donor abilities could have an impact similar to NHCs.

A synthetic route to such a nitrogen donor is shown in Scheme 2. The alkylation of 4-(isopropylamino)pyridine at the pyridine nitrogen atom with MeI and subsequent deprotonation of the amino nitrogen atom with NaH provides **1** as a white, sublimable, toluene-soluble powder in 85% yield. Species **1** has two viable resonance structures that could describe its ground state. The imine form has minimized charge separation, whereas the zwitterionic form benefits from aromatic stabilization.



Scheme 2. Synthesis of donor **1** and its structure.[14]

The solid-state structure of **1** was determined by X-ray crystallography, and an ORTEP depiction is shown in Scheme 2. The C(4)–N(1) bond length of 1.3044(15) Å confirms that **1** displays considerable imine character; typical bond lengths for single and double C–N bonds are 1.47 and 1.28 Å, respectively. Likewise, the C(4)–C(5) bond of 1.4532(16) Å is longer than a typical aromatic C–C bond, and the C(5)–C(6) bond of 1.3474(17) Å is much shorter. The C(6)–N(2) bond of 1.3709(15) Å is longer than the expected 1.34 Å for pyridine N–C bonds. The ^{1}H NMR spectrum of **1** in C_6D_6 displays four proton environments for the nitrogen-containing ring, owing to the considerable double-bond character of the C(4)–N(1) bond. Irrespective of this considerable imine character, the reactivity of **1** resembles that of an amido salt, as exemplified by its behavior as a strong base in aqueous solution.

Adducts generated from $[\{(CO)_2Rh(\mu\text{-}Cl)\}_2]$ have been used to determine the donor properties of NHCs by measurement of the CO stretching frequencies.[15] To provide a comparison, donor **1** was treated with half an equivalent of $[\{(CO)_2Rh(\mu\text{-}Cl)\}_2]$ to generate *cis*-$[(CO)_2RhCl(i\text{PrNC}_5H_4\text{NMe})]$ (**2**, Scheme 3). The solid-state structure of **2** was determined by X-ray crystallography and confirms binding of the nitrogen donor to the rhodium center with minimal perturbation of the C–N and C–C bond lengths compared to those of the free ligand **1**. The IR spectrum of **2** displays two CO stretching frequencies at 2077 and 1998 cm^{-1} (av 2038 cm^{-1}). By this measure, **1** is a significantly stronger donor than the pyridine analogue, which displays an average $\nu_{CO} = 2052$ cm^{-1}.[16] Remarkably, the average ν_{CO} value for **2** is

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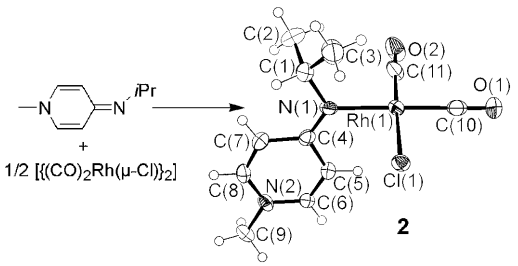


Scheme 3. Synthesis of the rhodium carbonyl adduct **2** and its structure.[14]

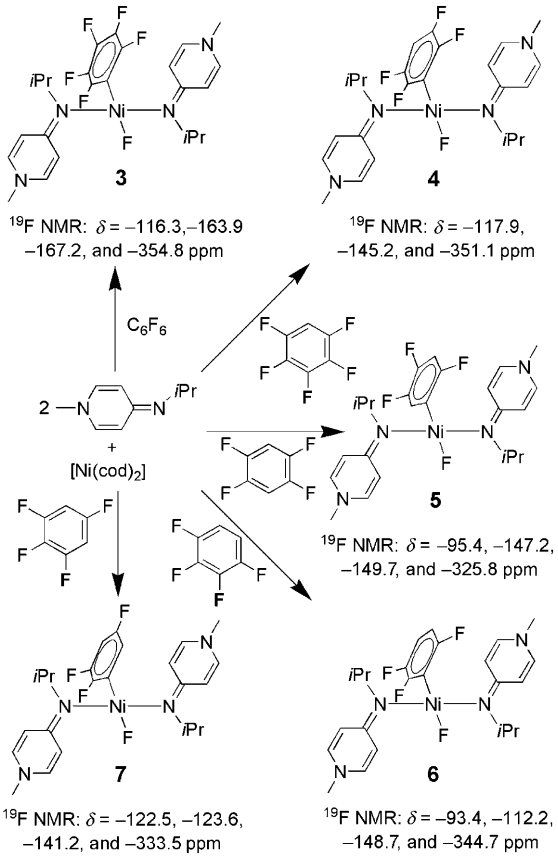
similar to that of the analogous complex of the N-heterocyclic carbene **A**, which displays ν_{CO} values of 2081 and 1996 cm^{-1} (av 2039 cm^{-1}).[17] This comparison indicates that the donor properties of **1** could resemble those of the NHCs.

To test the ability of these ligands to aid in the oxidative addition of challenging substrates, we investigated the activation of the strong and relatively inert C–F bonds[18–21] in fluorinated aromatics by nickel(0).[22–30] It is known that sources of the $\{(PEt_3)_2Ni\}$ moiety react with the tetrafluorobenzenes, but the reaction takes weeks at room temperature and can provide unwanted byproducts by rapid and reversible C–H bond activation.[31] Very recently it has been shown that the use of N-heterocyclic carbenes rather than phosphines as the ancillary ligand in these reactions allows for more rapid selective activation of C–F bonds in a variety of polyfluorobenzene species; however, to date no nickel complex capable of the selective activation of the tetrafluorobenzenes has been reported.[32]

As monitored by ^{1}H NMR spectroscopy, toluene solutions of $[Ni(cod)_2]$ (cod = 1,5-cyclooctadiene) and **1** showed no significant replacement of the 1,5-cyclooctadiene donors, as might be expected for a hard donor such as **1**. However, solutions of two equivalents **1** and one equivalent $[Ni(cod)_2]$ react over the course of 0.5–5 h at room temperature with C_6F_6, C_6F_5H, 1,2,4,5-, 1,2,3,4-, and 1,2,3,5-tetrafluorobenzene to form C–F bond-activated products **3**–**7**, respectively (Scheme 4). The products precipitated from the reaction mixtures as red crystalline solids and were isolated in 70–80 % yields.

All three components (Ni^0 source, ligand, and fluorinated substrate) are necessary to observe a reaction; no reaction was observed in solutions of either $[Ni(cod)_2]$ with the polyfluoroaromatics or **1** with the polyfluoroaromatics. Also, no reaction was observed in these systems when alternate nitrogen donors such as bipyridine or the imine *t*BuCHNPh[33] were used in place of **1**.

The solid-state structure of **3** was determined by X-ray crystallography, and an ORTEP depiction is shown in Figure 1. Product **3** is square-planar, with the ancillary ligands *trans* disposed. The nitrogen-containing and pentafluorophenyl rings all lie out of the coordination plane, and the isopropyl substituents of the ancillary ligands are situated on opposites faces of the square plane. The Ni(1)–N(1) bond length is 1.9256(15) Å, which lies within the range of nickel amide bonds (1.93–1.82 Å)[34] and is shorter than nickel imine bonds, which are typically longer than 2.0 Å.



Scheme 4. C–F bond activation with C_6F_6, C_6F_5H, and all three isomers of $C_6F_4H_2$. Site of selective activations shown in bold; chemical shifts from $^{19}F\{^1H\}$ NMR spectra are given with respect to $CFCl_3$ at $\delta = 0.0$ ppm.

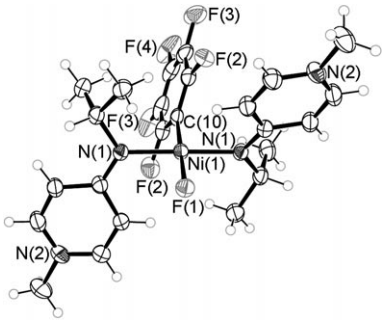


Figure 1. Structure of **3** as determined by X-ray crystallography.[14] Selected bond lengths [Å]: Ni(1)–N(1) 1.9256(15), Ni(1)–F(1) 1.8589(15), Ni(1)–C(10) 1.903(3).

Both the ^{1}H and $^{19}F\{^1H\}$ NMR spectra for **3**–**7** in CD_2Cl_2 are consistent with regioselective C–F bond activation, with no detectable impurities or byproducts. The $^{19}F\{^1H\}$ shifts for **3**–**7** are summarized in Scheme 3. Notably, the chemical shift for the fluoride resonance is dramatically affected by the substitution pattern of the fluoroaryl group, with the presence *ortho* and *meta* fluorine substituents having a larger effect than the *para* fluorine substituents on the fluoride shift. The similarity of the ^{1}H NMR spectra for the ancillary ligand

resonances in **3**–**7** suggests that these complexes are isostructural to the structurally characterized **3**.

The site of activation in **4**–**7** was readily confirmed by reaction with a solution of 10% HCl in D_2O and subsequent extraction into C_6D_6 and filtration through silica gel to remove any protonated **1** and nickel-containing byproducts. The site of deuteration in the resultant fluorobenzene derivatives was readily determined by NMR spectroscopy by using the deuterium isotope effect on the ^{19}F chemical shifts. The regioselectivity observed is identical to the preferred products of typical nucleophilic aromatic substitution reactions with these substrates, but with significantly improved regioselectivity.[35]

This donor set facilitates regioselective C–F bond activation, which includes the first example of selective C–F bond activation of the tetrafluorobenzenes by a nickel complex. These results illustrate the strong N-heterocyclic-carbene-like σ-donor properties of **1** and the ability of this hard ligand to facilitate difficult oxidative additions. In light of the remarkable scope and impact of N-heterocyclic carbenes, the investigation of these simple nitrogen donors as alternative ligands in similar applications is warranted.

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