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Nickel-Catalyzed *ortho*-Selective Hydrodefluorination of *N*-Containing Heterocycle-Polyfluoroarenes

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An effective and facile method for preparation of partially fluorinated aromatics via Nickel catalyzed, chelation-assisted *ortho* selective hydrodefluorination of polyfluoroarnes with triethylsilane has been developed, in which *N*-containing heterocycles were used as directing groups. The advantage of this protocol is its simple catalytic system with use of inexpensive and readily available $NiCl_2•6H_2O$ as a catalyst.

Keywords catalytic C—F activation, hydrodefluorination, nickel, polyfluoroarenes, triethylsilane

Introduction

Partially fluorinated aromatics are an important class of fluorinated compounds owning to the presence of such moieties in a wide range of biologically active compounds and functional materials of importance in various application fields.[1] Hence, it is of great interest to access such fluorinated compounds. Among the known methods of preparation of partially fluorinated aromatics,[2,3] the selective C—F activation and functionalization of polyfluoroarenes catalyzed by transition-metal represents one of the most attractive approach,[4] as the polyfluoroarenes are more readily available and cheaper than their mixed halo or organometal counterparts. In particular, the catalytic hydrodeflurorination (HDF) of polyfluoroarenes is the simplest approach to obtain partially fluoroarenes that are difficult to obtain otherwise.[5] However, the selective transition-metal-catalyzed C—F activation remains a challenge due to the strong bond dissociation energies. Although many efforts have been made in this area in the past few years, most of the developed methods for selective transition-metal-catalyzed HDF of polyfluoroarenes mainly focus on the mechanistic understanding of the HDF cycle.[6] Furthermore, in most of the cases, only the C—F bonds in the *para*-position to the substituent undergo reduction.[7] Therefore, to overcome these limitations for widespread applications, it is highly desirable to develop new catalytic system and strategy.

Very recently, we developed an efficient method for *ortho* selective hydrodefluorination of polyfluoroarenes, in which Pd was used as a catalyst and *N*-containing heterocycles were employed as directing groups (Scheme 1a).[8]

However, from the viewpoint of practicality and cost effectiveness, the use of less expensive and abundant metal catalysts, such as nickel, to execute such C—F bond activation would be promising.[9] To continue our research, herein, we describe a nickel-catalyzed chelation assisted hydrodefluorination of *N*-heterocycles substituted polyfluoroarenes with triethylsilane (Scheme 1b). This protocol provides an effective access to partially fluorinated aromatics that are important in photoelectronic devices (Figure 1).[10]

Experimental

General procedure for Ni-catalyzed *ortho*-selective hydrodefluorination of *N*-containing heterocycle-fluoroarenes with triethylsilane.

To a septum capped 25 mL of sealed tube were added $NiCl_2•6H_2O$ (5 mg, 5 mol%), Phen (4 mg, 5 mol%), Zn dust (2.6 mg, 10 mol%), and *N*-containing heterocycle-polyfluoroarene **1** (0.4 mmol), followed by DMF (2.0 mL) with stirring. Triethylsilane (96 μL, 0.6 mmol, 1.5 equiv.) was then added subsequently. The sealed tube was screw capped and heated to 100 ℃ (oil bath). After stirring for 8 h, the reaction mixture was

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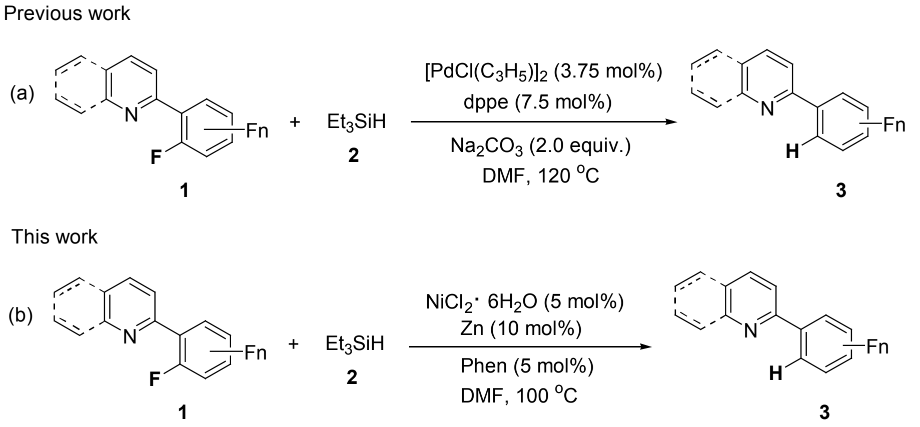
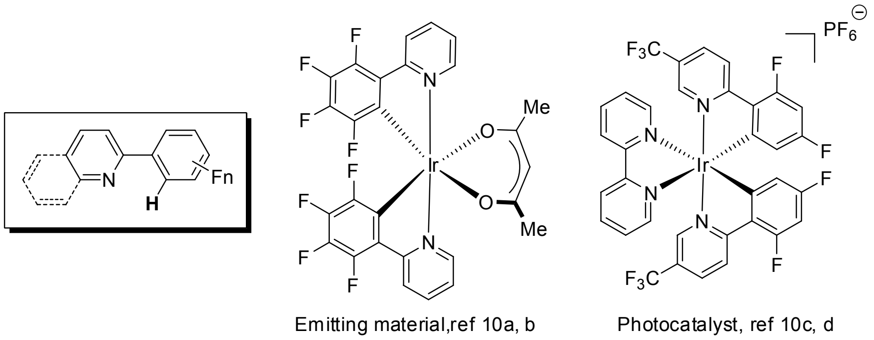
Scheme 1 Transition-metal-catalyzed *ortho*-selective hydrodefluorination of *N*-heterocycles substituted polyfluoroarenes with triethylsilane





Emitting material,ref 10a, b

Photocatalyst, ref 10c, d

Figure 1 *N*-Containing heterocyle-fluoroaromatics in photoelectronic materials.

cooled to room temperature, and diluted with ethyl acetate, washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified with silica gel chromatography to provide pure product.

Results and Discussion

In view of the importance of 2-(2,3,4,5-tetrafluorophenyl)pyridine **3a** in the light-emitting devices, we began our studies by choosing 2-(perfluorophenyl)pyridine **1a** as the model substrate that can be easily prepared by the cross-coupling of pentafluoroarene with 2-halopyridine.[2] Initially, a cheap and readily available $NiCl_2 \cdot 6H_2O$ was used as a precatalyst. However, only 9% of hydrodefluorinated **3a** was observed when the reaction was carried out with **1a** (1.0 equiv.), Et_3SiH (1.5 equiv.), $NiCl_2 \cdot 6H_2O$ (5 mol%) in DMF at 100 ℃ for 6 h (Table 1, Entry 1). Considering that an active Ni(0) catalyst may be involved in the catalytic cycle, which undergoes oxidation of C—F bond *ortho* to the pyridyl group, Zn dust (10 mol%) was added to reaction (Table 1, Entry 2). To our delight, the yield of **1a** was improved to 23% yield (determined by ^{19}F NMR) albeit formation of 7% yield of dihydrodefluorinated product **4a**. To further improve the reaction efficiency, diamine ligand 1,10-phenanthroline (Phen) that can stabilize the soluble Ni(0) complexes by chelation and increase the electron density at the nickel center was examined, providing **3a** in 62% yield (determined by ^{19}F NMR) with trace amount of **4a** observed (Table 1, Entry 3). Prolonging the reaction time to 8 h benefited the reaction efficiency with 60% isolated yield obtained (Table 1, Entry 4). Encouraged by these results, a series of reaction parameters, such as ligands, Ni catalysts, and the loading amount of Zn dust were investigated (Table 1, Entries 5—15). It turned out that Phen is the optimized one, other ligands, such as bipy and dppe, were less effective (Table 1, Entries 5, 6). Among the tested Ni catalysts, $NiCl_2$ provided desired product **3a** in comparable yield (Table 1, Entry 8). $Ni(dppp)Cl_2$ showed the best catalytic effect, but 27% of dihydrodefluorinated **4a** was formed (Table 1, Entry 12). The loading amount of Zn dust also influenced the reaction efficiency. Decreasing Zn dust from 10 mol% to 5 mol% led to lower yield (Table 1, Entry 14). Similar result was also observed by increasing amount of Zn dust to 20 mol% due to formation of 21% yield of dihydrodefluorinated product **4a** (Table 1, Entry 15). Additionally, decreasing the reaction temperature to 90 ℃ led to diminished yield as well (Table 1, Entry 16). The absence of Ni-catalyst failed to give any desired product (Table 1, Entries 18—20), thus demonstrating that Ni species is involved in the catalytic cycle.

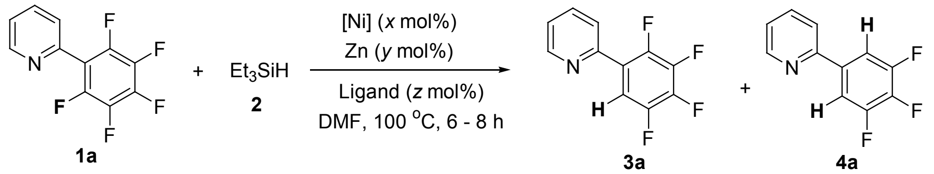
To demonstrate the pivotal role of 2-pyridyl group in this Ni-catalyzed *ortho* selective hydrodefluorination, the investigation of 2,3,4,5,6-pentafluoro-4'-methyl-1,1'-biphenyl **5** under the optimized reaction conditions was performed (Scheme 2a). However, no desired hydrodefluorinated product **6** was observed. Furthermore, the use of 3-(2-fluorophenyl)pyridine **7** failed to give compound **8** either (Scheme 2b). Thus, these findings demonstrated that the 2-pyridyl group indeed functionalizes as a directing group to chelate Ni species and facilitates the catalytic cycle.

Given the low cost and commercial availability of $NiCl_2$•6H_2O, a variety of *N*-containing heterocycle-fluoroarenes **1**[11] were examined under the reaction conditions as shown in Table 1 entry 4. Substrates bearing functionalized pyridyl or quinolinyl groups underwent the reaction smoothly, providing their corresponding *ortho* hydrodefluorinated aromatics in moderate to good yields with high regioselectivity (Table 2). Interestingly, fluoroarenes bearing less fluorine atoms afforded higher yields, such as difluoroarenes **1i** and **1j** (Table 2, **3i** and **3j**). In particular, for **1j** a good yield (81%) was obtained (Table 2, **3j**). This is in sharp contrast to our previous results using Pd-catalyst, in which difluoroarenes **1i** and **1j** are 'inert' substrates,[8] thus featuring the advantages of Ni-catalyst. In addition, using sequential C—F activation strategy, the dihydrodefluorinated **3f** can also be obtained in moderate yield from **3c** (Table 2, **3f**), providing a facile access to partially fluorinated aromatics that are difficult to prepare otherwise. However, for **3c** and **3d**, Ph_3SiH was used due to formation of a mixture of mono- and dihydrodefluorinated products when Et_3SiH was employed (Table 2, **3c** and **3d**).

Conclusions

In conclusion, we have developed a Ni-catalyzed *ortho*-selective hydrodefluorination of *N*-containing heterocycle-fluoroarenes with silane, which provides an effective and facile access to partially fluorinated

Table 1 Optimization of Ni-catalyzed *ortho*-selective C—F activation of **1a** with triethylsilane^a



Entry	[Ni] (x)	Zn (y)	Ligand (z)	**3a**, yield^b/%	**4a**, yield^b/%
1^c	$NiCl_2$•6H_2O (5)	—	—	9	ND
2^c	$NiCl_2$•6H_2O (5)	10	—	23	7
3^c	$NiCl_2$•6H_2O (5)	10	Phen (5)	62	—
4	$NiCl_2$•6H_2O (5)	10	Phen (5)	75 (60)	6
5	$NiCl_2$•6H_2O (5)	10	Bipy (5)	48	—
6	$NiCl_2$•6H_2O (5)	10	dppe (5)	61	—
7	$Ni(OAc)_2$•4H_2O (5)	10	Phen (5)	65	—
8	$NiCl_2$ (5)	10	Phen (5)	71	7
9	$Ni(acac)_2$ (5)	10	Phen (5)	trace	—
10	$Ni(dppf)Cl_2$ (5)	10	Phen (5)	68	—
11	$Ni(PPh_3)_2Cl_2$ (5)	10	Phen (5)	73	9
12	$Ni(dppp)Cl_2$ (5)	10	Phen (5)	73	27
13	$NiCl_2$•6H_2O (2.5)	10	Phen (2.5)	38	—
14	$NiCl_2$•6H_2O (5)	5	Phen (2.5)	46	—
15	$NiCl_2$•6H_2O (5)	20	Phen (2.5)	50	21
16^d	$NiCl_2$•6H_2O (5)	10	Phen (5)	50	—
17	$NiCl_2$•6H_2O (5)	—	Phen (2.5)	7	—
18	—	—	Phen (2.5)	NR	—
19	—	10	—	NR	—
20	—	10	Phen (2.5)	NR	—

^{a} Unless otherwise noted, the reaction was carried out by using **1a** (0.4 mmol, 1 equiv.), Et_3SiH **2** (1.5 equiv.) in DMF (2 mL) for 8 h. ND, not determined. NR, no reaction. ^{b} NMR yield determined by ^{19}F NMR using fluorobenzene as internal standard and number in parenthesis is isolated yield. ^{c} Reaction conducted for 6 h. ^{d} Reaction conducted at 90 ℃.

Scheme 2 Reaction of 2,3,4,5,6-pentafluoro-4'-methyl-1,1'-biphenyl **5** or 3-(2-fluorophenyl)pyridine **7** with triethylsilane in the presence of nickel

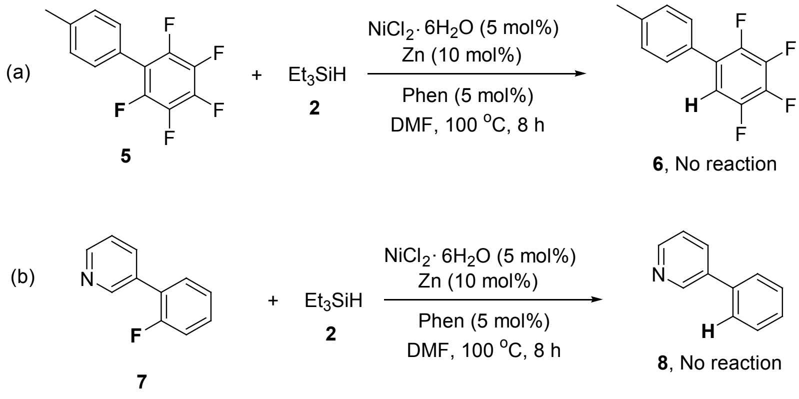
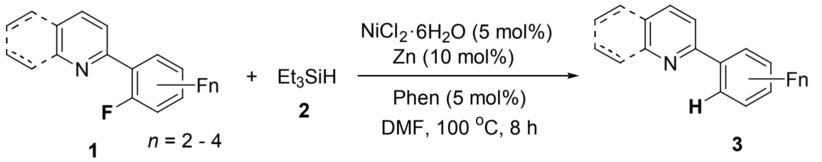
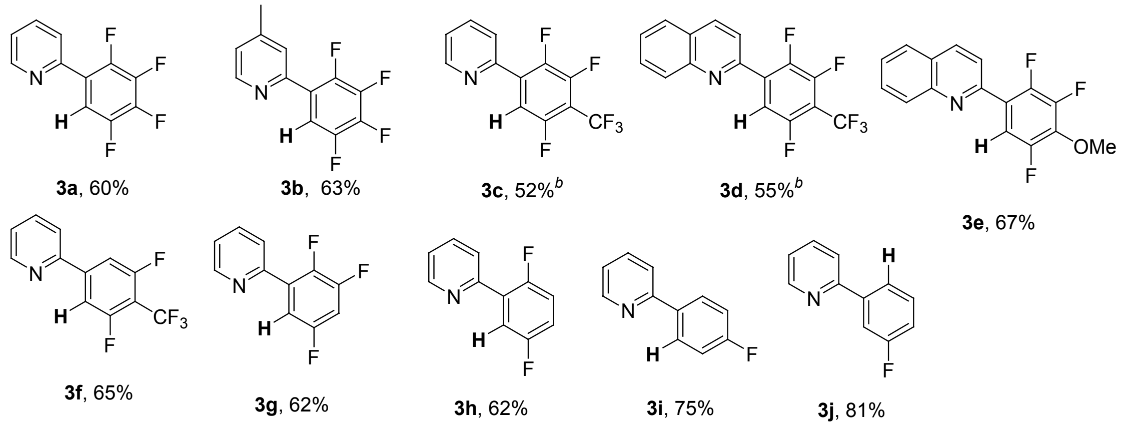


Table 2 Ni-catalyzed *ortho* selective hydrodefluorination of *N*-containing heterocycle-fluoroarenes **1**[a]





3a, 60%
3b, 63%
3c, 52%[b]
3d, 55%[b]
3e, 67%
3f, 65%
3g, 62%
3h, 62%
3i, 75%
3j, 81%

[a] Unless otherwise noted, the reaction was carried out by using **1** (0.4 mmol, 1 equiv.), Et_3SiH **2** (1.5 equiv.) in DMF (2 mL) for 8 h. All reported reaction yields are isolated yields. [b] 1.5 equiv. of Ph_3SiH was used.

aromatics that are difficult to prepare otherwise. The advantage of this reaction is its simple catalytic system with use of inexpensive and readily available $NiCl_2•6H_2O$ as a catalyst. Further studies to expand the substrates scope and uncover the reaction mechanism are currently in progress.

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[11] *N*-Containing heterocycle-fluoroarene **1** can be easily prepared through tansitionmetal-catalyzed cross-coupling of commercially available polyfluoroarenes with heteroaryl halides or tosylates, see ref. 2c and 3d.

(Lu, Y.)