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Catalytic C−C Bond Formation Accomplished by Selective C−F Activation of Perfluorinated Arenes

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Carbon−carbon bond formation reactions are important processes in chemistry because they provide key steps in the preparation of complex molecules starting from simple precursors. The synthesis of aryl and biaryl systems via transition-metal-catalyzed cross-coupling reactions has been well developed over the past decades.[1] Among all the possible organometallics used as nucleophilic reagents, Grignard (Kumada coupling)[2] and organozinc reagents (Negishi coupling)[3] as well as tin (Stille coupling)[4] and boron derivatives (Suzuki−Miyaura coupling)[5] have been most frequently used for cross-coupling reactions of aryl compounds. Although aryl iodides, bromides, and triflates are the most commonly used electrophiles, aryl chlorides, hitherto regarded as inert to palladium-catalyzed cross-coupling reactions, have been shown to be also effective participants in the past few years.[6]

Synthetically useful routes for the generation of fluoroorganics by transition-metal-mediated conversions of aromatic C−F bonds into C−C bonds are barely developed, which is mainly due to the enormous bond strength of C−F bonds as well as the absence of transition metal complexes that readily activate C−F bonds.[7−9] Although Kumada and co-workers reported a nickel-catalyzed coupling reaction of fluorobenzene and isopropyl magnesium chloride in the early 1970s[8a] and Hermann and co-workers published Kumada coupling reactions of monofluorine aromatics to connect two sp^2-hybridized carbon atoms, similar reactions using polyfluorinated arene electrophiles remain elusive. Almost all of the transformations known to date consist of cross-coupling reactions to convert *mono*fluoroarenes into nonfluorinated derivatives.[8] Ackermann and co-workers, for example, have shown only recently that catalytic systems which are active for nickel-catalyzed Kumada cross-coupling reactions of monofluoroarenes are not active for polyfluorinated compounds such as hexafluorobenzene.[8e] Two special cases of catalytic active systems that can accomplish cross-coupling of highly fluorinated pyridines and pyrimidines have been published by Braun et al.[9]

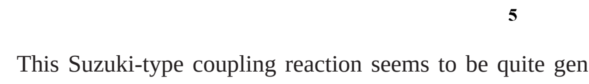
We reported the synthesis and characterization of the NHC (N-heterocyclic carbene)-stabilized nickel complex [Ni$_2$(^{i}Pr$_2$Im)$_4$(COD)] **1** (^{i}Pr$_2$Im = 1,3-di(isopropyl)imidazol-2-ylidene) only recently.[10] This compound is a source of the [Ni(^{i}Pr$_2$Im)$_2$] complex fragment in stoichiometric as well as catalytic transformations. We have demonstrated that **1** is an excellent catalyst for the catalytic insertion of diphenyl acetylene into the 2,2′-C−C bond of biphenylene and also very efficient in the activation of hexafluorobenzene. We now report the usage of [Ni$_2$(^{i}Pr$_2$Im)$_4$(COD)] **1** in Kumada and Suzuki−Miyaura-type cross-coupling reaction using polyfluorinated arenes as electrophiles.

Since **1** activates the C−F bond of hexafluorobenzene very efficiently, we were encouraged to further investigate C−F activation reactions of fluorinated arenes with **1**, putting an emphasis on the regio- and chemoselectivity of this transformation. The reaction of **1** with different fluorinated aromatic compounds in THF, benzene, or toluene occurs with a high chemo- and regioselectivity. As shown in Scheme 1, the reaction of octafluorotoluene and decafluorobiphenyl with **1** yields *trans*-[Ni(^{i}Pr$_2$Im)$_2$(F)(4-(CF$_3$)-C$_6$F$_4$)] **2** and *trans*-[Ni(^{i}Pr$_2$Im)$_2$(F)(4-(C$_6$F$_5$)C$_6$F$_4$)] **3**. Performed on NMR scale, these reactions are quantitative according to ^{1}H and ^{19}F NMR spectroscopy.

The ^{19}F NMR spectrum of **2** reveals three sets of signals at −55.24, −115.74, and −146.18 ppm for the perfluorinated tolyl ligand and, most significantly, a resonance at −372.74 ppm for the fluoride ligand. For compound **3**, five sets of resonances were observed for the nonafluorobiphenyl substituent and a singlet at −370.53 ppm for the fluoride ligand. The carbene ligands of both compounds gave rise to two sets of signals for the methyl groups and one septet for the ^{i}Pr substituent as well as a singlet for the olefinic protons in the ^{1}H NMR spectra. Accordingly, highly symmetric reaction products were formed, in which the carbene ligands are located in *trans* positions with respect to each other and the perfluorinated arenyl ligand is bound in *trans* position to the CF$_3$ and C$_6$F$_5$ groups, respectively. This was confirmed by an X-ray analysis of compound **2** (see Figure 1), which revealed a square planar coordinated nickel atom, in which both carbene ligands are mutually in *trans* position to each other and which corroborates C−F activation *trans* to the CF$_3$ group of perfluorotoluene. In neither case, the product of a multiple insertion of the [Ni(^{i}Pr$_2$Im)$_2$] complex fragment into C−F bonds of these substrates was observed under the conditions employed.

Since the first results concerning the reactivity of **2** and **3** and the pentafluorophenyl analogue [Ni(^{i}Pr$_2$Im)$_2$(F)(C$_6$F$_5$)] **4** have shown that the fluoride ligand in these compounds can be easily replaced with anionic reagents, we were encouraged to investigate the catalytic performance of **1** in Kumada and Suzuki-type coupling reactions.

The catalytic reaction of perfluorotoluene with phenyl boronic acid using 2 mol % of **1** as a catalyst afforded in a clean reaction the coupling product (eq 1), which was characterized by mass spectroscopy, ^{1}H and ^{19}F NMR spectroscopy, as well as X-ray structure analysis (see Supporting Information). This reaction strongly depends on the reaction conditions employed. The usage of NEt$_3$ as a base leads after a reaction time of 12 h at 60 °C to an isolated yield of 83%. This yield significantly decreases when K$_2$CO$_3$ (54%), KF (59%), or NaOH/KF (44%) was used.



(1)

5

This Suzuki-type coupling reaction seems to be quite general, and different boronic acids have been employed so far. Using 2 mol % of **1** as a catalyst, NEt$_3$ as a base, and reaction times of

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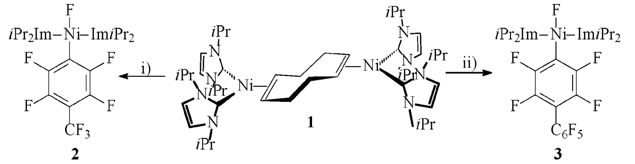
Scheme 1. Reaction of $[Ni_2({}^iPr_2Im)_4(COD)]$ (**1**) with C_7F_8 and $C_{12}F_{10}$[a]



[a] Reagents and conditions: (i) C_7F_8, THF, rt, 75%; (ii) $C_{12}F_{10}$, THF, rt, 54%.

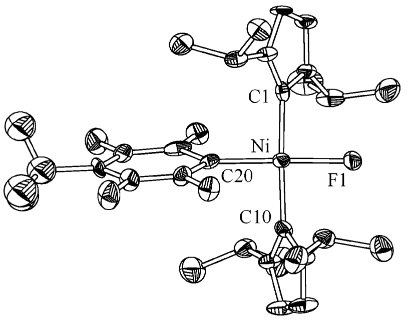
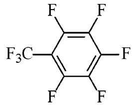
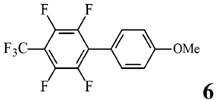
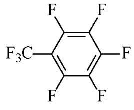
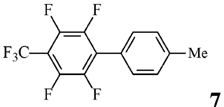
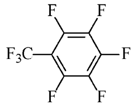
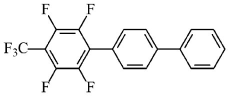
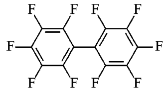
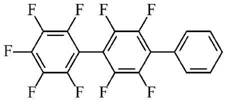


Figure 1. ORTEP diagram of the molecular structure of $[Ni({}^iPr_2Im)_2(F)(4\text{-}(CF_3)C_6F_4)]$ (**2**) in the solid state (ellipsoids set at 40% probability level). Hydrogen atoms have been omitted for clarity. Bond lengths (Å) and angles (deg): Ni−F(1) 1.856(4), Ni−C(1) 1.932(8), Ni−C(10) 1.911(8), Ni−C(20) 1.870(8); F(1)−Ni−C(1) 89.1(2), F(1)−Ni−C(10) 88.0(3), F(1)−Ni−C(20) 178.6(3), C(1)−Ni−C(10) 175.0(3), C(1)−Ni−C(20) 92.0(3), C(10)−Ni−C(20) 91.0(3).

Table 1. Suzuki Cross-Coupling Reactions of Perfluorinated Arenes[a]

Fluoroarene	Product	Yield
	 **6**	66 %
	 **7**	50 %
	 **8**	44 %
	 **9**	66 %

[a] Reaction conditions: For entries 1−3: 2 mol % of **1**, 3 equiv of NEt_3, THF, 12 h, 60 °C; for entry 4: 2 mol % of **1**, 3 equiv of K_2CO_3, THF, 18 h, 60 °C. For all entries, yields of the isolated compounds are given.

12 h at 60 °C as standard reaction conditions, we accomplished the cross-coupling of octafluorotoluene with 4-methoxyphenyl boronic acid, 4-methylphenyl boronic acid, and *p*-biphenyl boronic acid in 66, 50, and 44% yield, respectively, and the coupling of perfluorinated biphenyl with phenylboronic acid in 66% isolated yield (see Table 1). In all cases, the fluoro substituents in *trans* position of the CF_3 or C_6F_5 group are substituted with aryl groups. No coupling products in *ortho* and *meta* positions have been detected in the ^{19}F NMR spectra of the crude products.

Compound **1** is also catalytically active for Kumada-type cross-coupling reactions of polyfluorinated arenes with Grignard reagents, albeit the yields of these transformations are generally lower. The synthesis of previously unknown compound **7**, for example, starting from perfluorotoluene and 2.5 equiv of *para*-tolyl magnesium bromide under similar conditions as employed for the Suzuki coupling reaction (2 mol % of catalyst **1**, THF, 12 h, 60 °C) provided **7** in only 26% isolated yield. GC−MS data of the crude product revealed a large amount of homocoupling product of the Grignard reagent.

In conclusion, we report here the first example of a catalytically active system for Suzuki-type cross-coupling reactions of perfluorinated arenes such as octafluorotoluene and perfluorobiphenyl, which combines C−F activation of these substrates efficiently with C−C coupling reactions. Although C−F activation appears to be quite general in this system, it is necessary to optimize each reaction separately. Work to expand the scope of this metal-catalyzed cross-coupling reaction of aryl fluorides and applying this concept to other transformations is currently in progress.

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Supporting Information Available: Crystallographic data of **2** and **5** and experimental preparations of the compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Tsuji, J. *Palladium Reagents and Catalysis*; Wiley and Sons: Chichester, U.K., 1995. (b) Diederich, F.; Stang, P. J. *Metal-Catalyzed Cross-Coupling Reactions*; VCH: Weinheim, Germany, 1998. (c) Miyaura, N., Ed. Cross-Coupling Reactions. A Practical Guide. In *Topics in Current Chemistry*; Springer-Verlag: Berlin, Germany, 2002; Vol. 219. (d) de Meijere, A., Diederich, F., Eds. *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; Wiley-VCH: Weinheim, Germany, 2004.
(2) (a) Tamao, K.; Sumitani, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94*, 4374−4376. (b) Knochel, P.; Sapountzis, I.; Gommermann, N. In *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; de Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, Germany, 2004; pp 671−698.
(3) Negishi, E.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979−2017.
(4) (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508−524. (b) Espinet, P.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4704−4734.
(5) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483. (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147−168. (c) Suzuki, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; VCH: Weinheim, Germany, 1998; pp 49−97. (d) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359−1469.
(6) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176−4211.
(7) (a) Burdeniuc, J.; Jedlicka, B.; Crabtree, R. H. *Chem. Ber./Recl.* **1997**, *130*, 145−154. (b) Kiplinger, J. L.; Richmond, T. G.; Osterberg, C. E. *Chem. Rev.* **1994**, *94*, 373−431. (c) Richmond, T. G. *Top. Organomet. Chem.* **1999**, *3*, 243−269. (d) Braun, T.; Perutz, R. N. *Chem. Commun.* **2002**, 2749−2757. (e) Jones, W. D. *Dalton Trans.* **2003**, 3991−3995.
(8) (a) Kiso, Y.; Tamao, K.; Kumada, M. *J. Organomet. Chem.* **1973**, *50*, C12. (b) Böhm, V. P. W.; Gsöttmayr, C. W. K.; Weskamp, T.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 3387−3389. (c) Mongin, F.; Mojovic, L.; Giullamet, B.; Trécourt, F.; Quéguiner, G. *J. Org. Chem.* **2002**, *67*, 8991−8994. (d) Dankwardt, J. E. *J. Organomet. Chem.* **2005**, *690*, 932−938. (e) Ackermann, L.; Born, R.; Spatz, J. H.; Meyer, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 7216−7219. (f) Widdowson, D. A.; Wilhelm, R. *Chem. Commun.* **1999**, 2211−2212. (g) Widdowson, D. A.; Wilhelm, R. *Chem. Commun.* **2003**, 578−579. (h) Kim, Y. M.; Yu, S. *J. Am. Chem. Soc.* **2003**, *125*, 1696−1697. (i) Lamm, K.; Stollenz, M.; Meier, M.; Görls, H.; Walther, D. *J. Organomet. Chem.* **2003**, *681*, 24−36.
(9) (a) Edelbach, B. L.; Kraft, B. M.; Jones, W. D. *J. Am. Chem. Soc.* **1999**, *121*, 10327. (b) Braun, T.; Perutz, R. N.; Sladek, M. I. *Chem. Commun.* **2001**, 2254−2255. (c) Steffen, A.; Sladek, M. I.; Braun, T.; Neumann, B.; Stammler, H.-G. *Organometallics* **2005**, *24*, 4057−4064.
(10) Schaub, T.; Radius, U. *Chem.—Eur. J.* **2005**, *11*, 5024−5030.

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