294 Organometallics **1999,** *18,* 294−296

Catalytic C−F Bond Activation of Nonactivated Monofluoroarenes

Robert J. Young, Jr., and Vladimir V. Grushin*

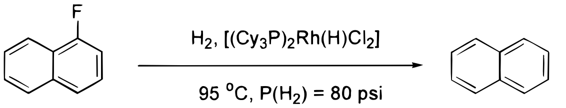
Central Research and Development, Experimental Station, DuPont de Nemours and Co., Inc.,[†] Wilmington, Delaware 19880-0328

Received October 29, 1998

Summary: Catalytic hydrogenolysis of the C−F bond in most unreactive monofluoroarenes readily occurs under mild conditions, in the presence of homogeneous and/or heterogeneous Rh catalysts generated from $[(Cy_3P)_2Rh(H)Cl_2]$*,* H_2*, and aqueous alkali.*

Carbon−fluorine bonds are the strongest bonds carbon can form.[1] Over the past decade, considerable progress has been made in the field of transition metal-promoted activation and cleavage of C−F bonds in organofluorine compounds.[2,3] However, examples of homogeneously catalyzed C−F bond activation reactions of fluoroarenes are scarce.[4−6] A few years ago, Aizenberg and Milstein[5] reported the first examples of a homogeneous, metal complex-catalyzed reductive defluorination of C_6F_6 to a mixture of C_6F_5H and $C_6F_4H_2$. Despite its thermodynamic stability, the C−F bond of hexafluorobenzene is highly reactive toward nucleophiles[2b,7] due to a remarkably low activation energy barrier (S_NAr). Very recently, Murai and co-workers[6] discovered the first Rh-catalyzed, chelation-assisted Si−F exchange reaction between disilanes and fluoroarenes activated by a ketone or oxazoline functionality ortho to the C−F bond. Nonactivated *mono*fluoroarenes are as thermodynamically stable as polyfluoroarenes but are incomparably more kinetically inert. Even under drastic conditions, fluoronaphthalenes, fluorobenzene, and their derivatives containing electron-donating groups remain unreactive toward nucleophiles and transition metal complexes, the Aizenberg−Milstein[5] and Murai[6] systems included. In this communication, we wish to report the first example of a transition metal-catalyzed hydrogenolysis of the C−F bond in monofluoroarenes, the most unreactive carbon−heteroatom single bond known. It is noteworthy that in most cases catalytic C−F activation of costly monofluoroarenes represents a considerable intellectual challenge[2] rather than a matter of practicality.

We found that 1-fluoronaphthalene reacted with H_2 in toluene in the presence of 40% NaOH and catalytic amounts of $[(Cy_3P)_2Rh(H)Cl_2]$ to give naphthalene (eq 1). Given the exceptionally poor reactivity of the substrate, the reaction occurred under mild conditions, i.e., 95 °C and 80 psi of H_2, furnishing naphthalene in >90% selectivity at 45% conversion (GC−MS) after 20 h.[8] Under rigorously oxygen-free conditions (see below), hydrogenolysis reaction 1 is *homogeneously* catalyzed, as determined by the mercury test.[9,10]



(1)

Fluorobenzene, 4-fluorotoluene, 3-fluoroanisole, and 4-fluoroaniline remained unreactive under similar *O_2-free conditions*.[11] Halobenzenes are known to exhibit lower reactivity toward metal complexes than halonaphthalenes; for example, chlorobenzene has been found 27 times less reactive than 1-chloronaphthalene in the hydroxycarbonylation reaction, catalyzed by [Ni-

---

[†] Contribution No. 7812.

(1) Cox, J. D.; Pilcher, G. *Thermochemistry of Organic and Organometallic Compounds*; Academic Press: London, 1970. McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493. Smart, B. E. In *The Chemistry of Functional Groups, Suppl. D*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1983; Chapter 14.

(2) For reviews, see: (a) Kiplinger, J. L.; Richmond, T. G.; Osterberg, C. E. *Chem. Rev.* **1994**, *94*, 373. (b) Burdeniuc, J.; Jedlicka, B.; Crabtree, R. H. *Chem. Ber./Recl.* **1997**, *130*, 145. (c) Richmond, T. G. *Topics Organomet. Chem.*, in press. (d) Also, see: Murphy, E.; Murugavel, R.; Roesky, H. W. *Chem. Rev.* **1997**, *97*, 3425.

(3) For most recent work in the area, see: Burdeniuc, J.; Crabtree, R. H. *Organometallics* **1998**, *17*, 1582, and references therein.

(4) (a) Kiso, Y.; Tamao, K.; Kumada, M. *J. Organomet. Chem.* **1973**, *50*, C12. (b) The $[(dmpe)NiCl_2]$/RLi system reported by Kiso, Tamao, and Kumada[4a] is unique, being equally reactive toward Ar−X bonds regardless of the nature of halogen X. In all other instances the reactivity of Ar−X toward electron-rich metal complexes decreases in the order $I > Br > Cl \gg F$.

(5) Aizenberg, M.; Milstein, D. *Science* **1994**, *94*, 359; *J. Am. Chem. Soc.* **1995**, *117*, 8674. For mechanistic studies of this catalytic system, see: Edelbach, B.; Jones, W. D. *J. Am. Chem. Soc.* **1997**, *119*, 7734.

(6) Ishii, Y.; Chatani, N.; Yorimitsu, S.; Murai, S. *Chem. Lett.* **1998**, 157.

(7) Clark, J. H.; Wails, D.; Bastock, T. W. *Aromatic Fluorination*; CRC Press: Boca Raton, FL, 1996.

(8) A few percent of 1,2,3,4-tetrahydronaphthalene and 5-fluoro-1,2,3,4-tetrahydronaphthalene also formed (GC−MS). Running the reaction under 135 psi of H_2 for 48 h, other things being equal, gave 90% conversion of 1-fluoronaphthalene. However, the higher pressure and prolonged reaction time resulted in substantial hydrogenation of the aromatic ring. According to the GC−MS data naphthalene (44%), tetrahydronaphthalene (38%), 5-fluoro-1,2,3,4-tetrahydronaphthalene (7%), and decahydronaphthalene (trace) were formed in this case.

(9) (a) Hamlin, J. E.; Hirai, K.; Millan, A.; Maitlis, P. M. *J. Mol. Catal.* **1980**, *7*, 543. Anton, D. R.; Crabtree, R. H. *Organometallics* **1983**, *2*, 855. Lin, Y.; Finke, R. G. *Inorg. Chem.* **1994**, *33*, 4891, and references therein. (b) For a detailed recent discussion of the problem of “is it homogeneous or heterogeneous catalysis?”, see: Weddle, K. S.; Aiken, J. D., III; Finke, R. G. *J. Am. Chem. Soc.* **1998**, *120*, 5653.

(10) A mixture of 1-fluoronaphthalene (1.494 g; 10.2 mmol), 40% NaOH (5 g), toluene (1 mL), $[(Cy_3P)_2Rh(H)Cl_2]$ (0.075 g; 0.1 mmol), and a drop of *mercury* in a 100 mL Fischer−Porter tube was carefully degassed (3 freeze−pump−thaw cycles) and pressurized with H_2 at 73 psi (20 °C). The pressure increased to 83 psi as the mixture was heated to 95 °C (oil bath). After the mixture was stirred at this temperature for 20 h the pressure had dropped to 55 psi. The pressure was released at room temperature, and hexane (20 mL) was added to the biphasic system upon stirring. GC−MS analysis of the organic phase revealed 45% conversion to naphthalene at >90% selectivity.[8] Similar results were obtained when the reaction was repeated in the absence of mercury metal. As the hydrogenolysis occurred, the aqueous phase stayed colorless and the organic layer was red, with no sign of Rh metal formation being observed.

(11) No reaction of PhF occurred even in the presence of nucleophilic (KI) and/or Lewis acid ($ErCl_3{\cdot}6H_2O$) promoters.

10.1021/om980887w CCC: $18.00

Scheme 1

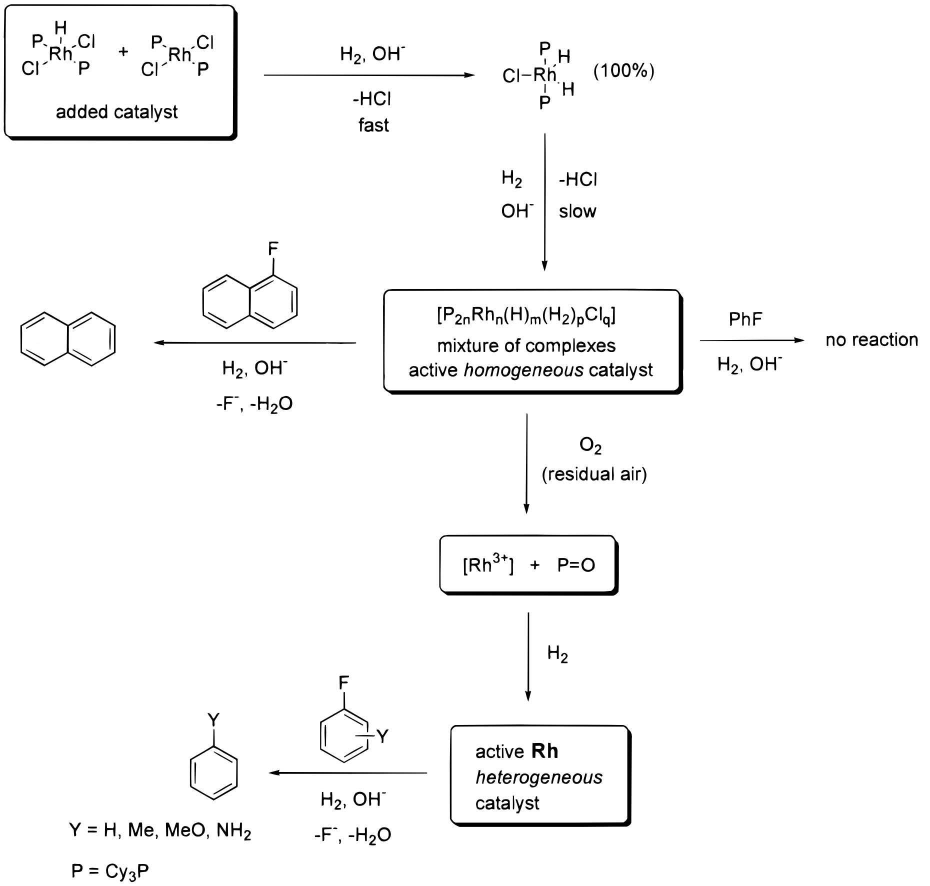


Table 1. Heterogeneous Rh-Catalyzed Reductive Defluorination of Fluoroarenes

$$\mathrm{ArF} + \mathrm{H_2} + \mathrm{NaOH} \xrightarrow{95\ ^{\circ}\mathrm{C}} \mathrm{ArH} + \mathrm{NaF} + \mathrm{H_2O}$$

Ar	$P(H_2)$, psi	time, h	O_2	Hg	conversion, %	catalytic turnover no.
Ph	40	25	+	−	55	88
Ph	40	28	+	+	<3	
Ph	40	3	−	−	<3	
Ph	135	21	−	−	<3	
4-MeC_6H_4	130	28	+	−	35	48
3-$MeOC_6H_4$	130	25	−	−	<3	
3-$MeOC_6H_4$	130	25	+	−	29	38
4-$MeOC_6H_4$	130	25	+	−	33	44
4-$NH_2C_6H_4$	130	25	+	−	95	150
4-$NH_2C_6H_4$	130	25	−	+	<3	

$(CO)_4]$.[12] However, when the pressurize-vent technique (4 cycles) was used instead of the freeze−pump−thaw method to purge the reaction mixture of air, a remarkably active catalytic system resulted and C−F hydrogenolysis smoothly occurred to produce benzene, toluene, anisole, and aniline from the corresponding fluoroarenes (Table 1).[13] All reactions were selective, as no biaryls and only trace amounts of benzene ring hydrogenation products were detected. The abrupt increase in the catalytic activity was obviously due to the presence of residual air in the system.[14] However, unlike reaction 1, all reductions presented in Table 1 were heterogeneously catalyzed,[15] as clearly indicated by a series of mercury tests.[9] No catalysis took place when both mercury metal and residual oxygen were present.

The catalytic C−F activation chemistry is outlined in Scheme 1. When $[L_2Rh(H)Cl_2]$ (often contaminated with $[L_2RhCl_2]$; L = Cy_3P or i-Pr_3P) is treated with hydrogen in the presence of OH^- under biphasic conditions, the quick (minutes) quantitative formation of $[L_2Rh(H)_2Cl]$ is observed.[16] Upon prolonged exposure to H_2/OH^-, this dihydride gradually disappears to furnish a mixture of electron-rich Rh hydrido species. The latter easily cleaves aromatic C−H and C−Cl bonds at room temperature and atmospheric pressure of H_2.[16] As we found in this work, the much stronger and more inert C−F bond of 1-fluoronaphthalene can also be activated by the

---

(12) Cassar, L.; Foa, M. *J. Organomet. Chem.* **1973**, *51*, 381.

(13) A mixture of ArF (15 mmol), 40% NaOH (5 g), and $[(Cy_3P)_2Rh(H)Cl_2]$ (0.075 g; 0.1 mmol) was placed in a 100 mL Fischer−Porter tube. The reactor was pressurized with H_2 to 60 psi at room temperature and then vented. After this procedure had been repeated three more times the reaction was run under conditions specified in Table 1. The mixture turned dark gray or almost black a few minutes after the reaction began. Ca. 0.1 mL (4−5 drops) of the organic phase was dissolved in $CDCl_3$ (0.7 mL), and the resulting solution was analyzed by ^1H NMR. Quantitative data were obtained by integrating signals or groups of signals (δ, ppm) as follows. Fluorobenzene/benzene: 7.0−7.2 (m, 3H, 3,4,5-C_6H_5F) vs 7.3−7.5 (m, 2H, 2,6-C_6H_5F + s, 6H, C_6H_6). 3-Fluoroanisole/anisole: 3.82 (s, 3H, $CH_3OC_6H_4F$) vs 3.84 (s, 3H, $CH_3OC_6H_5$). 4-Fluoroanisole/anisole: 3.80 (s, 3H, $CH_3OC_6H_4F$) vs 3.84 (s, 3H, $CH_3OC_6H_5$). 4-Fluoroaniline/aniline: 6.6−6.7 (m, 2H, 2,6-$NH_2C_6H_4F$) vs 7.1−7.3 (m, 2H, 2,6-$NH_2C_6H_5$). 4-Fluorotoluene/toluene: 2.38 (s, 3H, $CH_3C_6H_5$) vs 2.44 (s, 3H, $CH_3C_6H_4F$).

(14) There have been precedents for activation with oxygen in the metal-catalyzed hydrogenation chemistry. See, for example: Sommovigo, M.; Alper, H. *Tetrahedron Lett.* **1993**, *34*, 59.

(15) Heterogeneous systems for the hydrodefluorination of ArF with active metal *hydrides* have been reported. See: Caubère, P. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 599. Carfagna, C.; Musco, A.; Pontellini, R.; Terzoni, G. *J. Mol. Catal.* **1989**, *57*, 23. Li, H.; Liao, S.; Xu, Y. *Chem. Lett.* **1996**, 1059. Zhang, Y.; Liao, S.; Yu, D.; Shen, Q. *Synth. Commun.* **1997**, *27*, 4327.

(16) Grushin, V. V. *Acc. Chem. Res.* **1993**, *26*, 279.

same homogeneous catalyst, albeit requiring higher temperatures and pressures. However, C−F activation of less reactive YC_6H_4F (Y = H, Me, MeO, NH_2) was apparently beyond the scope of this system, under similar conditions.

In the presence of oxygen, the phosphine hydrido Rh species generated from $[L_2Rh(H)Cl_2]/H_2$/alkali[16] are easily oxidized to Rh^{3+} and LO.[17] In fact, Cy_3PO (δ = 50 ppm) was the only phosphorus-containing compound detected by ^{31}P NMR analysis of reaction mixtures originated from the C−F hydrogenolysis experiments conducted in the presence of residual air. Once oxidized, the phosphine oxide remains unchanged under the reaction conditions, whereas the Rh^{3+} is reduced with the hydrogen to a low-valent form. The latter is unstable in the absence of phosphine, clusterizing and eventually precipitating as catalytically active rhodium black. Remarkably, the activity of the Rh heterogeneous system depends on the nature of substrate used. Indeed, the conversion of 4-fluoroaniline was noticeably higher than those of fluorobenzene, 4-fluorotoluene, and fluoroanisoles under identical conditions (Table 1). The amino group may stabilize more catalytically active small Rh clusters, preventing them from further aggregation.

In conclusion, we have found the first example of hydrogenolysis of the otherwise unreactive C−F bond in 1-fluoronaphthalene, catalyzed by a *homogeneous* transition metal system. A small change in the reaction environment (traces of air) renders the homogeneous catalyst heterogeneous, with the concomitant increase in activity being sufficient for efficacious C−F activation of most robust fluorobenzenes.

OM980887W

---

[17] Grushin, V. V. Unpublished observations (1988−1989).