

Deaminative Fluorination of Anilines with Silicon Tetrafluoride: Utility of Silicon Tetrafluoride as a Fluorine Source

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Received July 30, 1997

Keywords: Fluorine / Silicon / Deaminative fluorination / Anilines / Fluoroarenes

Application of silicon tetrafluoride to deaminative fluorination of anilines as a fluorine source is investigated. A diazotization of anilines proceeds with silicon tetrafluoride and *t*-

butyl nitrite under mild condition and the following fluoro-dediazoniation affords fluoroarenes in good yields.

Silicon tetrafluoride (SiF₄) is obtained as a by-product in the manufacture of hydrogen fluoride (HF) from fluorite and in the wet-processing of phosphoric acid and phosphate fertilizers from phosphate rock^[1]. Concerning application of SiF₄ to organic synthesis, although its reactivity to organic compounds were somewhat investigated^[2], there had been very few reports about the utility of SiF₄ as a fluorine source, namely ring-opening of epoxides and halo-fluorination of alkenes^{[3][4]}.

During the course of our studies on fluorination reaction using potassium fluoride-hydrogen fluoride salts, we have recently disclosed that the combination of potassium hydrogen fluoride (KHF₂) and SiF₄ works as an efficient fluorinating agent that is the alternative to anhydrous hydrogen fluoride or amine-HF^{[5][6]}. In this paper, we report novel application of SiF₄ as a sole fluorine source to deaminative fluorination of aromatic amines (Scheme 1).

Scheme 1. Deaminative fluorination of aromatic amines



Concerning deaminative fluorination of anilines, it is a useful method for the synthesis of aromatic fluorides^{[7][8]}. The Baltz-Schiemann reaction is a representative method, but the isolation of diazonium fluoroborates is necessary and reproducibility of yields of the desired fluoroarenes is poor^[8]. To overcome these difficulties, a one-pot diazotization and fluoro-dediazoniation of anilines using HF or organic base-HF reagents, such as amine-HF, had been investigated^{[8][9][10][11][12]}. And recently, we reported a method using the combination of KHF₂ and SiF₄ instead of these HF reagents^[6]. However, these methods are not applicable to substrates containing groups sensitive to acidic condition or reactive with HF, such as cyano group. The method we describe here proceeds under mild condition and can be applied to the substrates possessing cyano group.

The deaminative fluorination of aniline was initially attempted (Table 1). Diazotization of aniline proceeded with SiF₄ and *t*-butyl nitrite, and by thermal decomposition of

the diazotization product, fluorobenzene was obtained in 69% yield from aniline (entry 1). When sodium nitrite or *n*-butyl nitrite was used as diazotizing agent, the diazotization did not proceed (entries 2 and 3). The best solvent for the diazotization reaction was dichloromethane, and the yield was low or the reaction did not proceed in the case of the other solvents (entry 4–7). Concerning the amount of SiF₄, the yields were almost same when the amount of SiF₄ was more than 1.0 molar equivalent to the substrate, although the yield diminished when less than 1.0 molar equivalent of SiF₄ was used (entry 8–12).

Table 1. Deaminative fluorination of aniline^[a]

Entry	Diazotizing agent	Amount of SiF ₄ (mmol)	Solvent	Yield ^[b] [%]
1	<i>t</i> -BuONO	1.5	CH ₂ Cl ₂	69
2	NaNO ₂	1.5	CH ₂ Cl ₂	0
3	<i>n</i> -BuONO	1.5	CH ₂ Cl ₂	2
4	<i>t</i> -BuONO	1.5	Et ₂ O	0
5	<i>t</i> -BuONO	1.5	<i>n</i> -hexane	0
6	<i>t</i> -BuONO	1.5	C ₆ H ₆	0
7	<i>t</i> -BuONO	1.5	CH ₃ CN	34
8	<i>t</i> -BuONO	0.5	CH ₂ Cl ₂	< 1
9	<i>t</i> -BuONO	0.75	CH ₂ Cl ₂	54
10	<i>t</i> -BuONO	1.0	CH ₂ Cl ₂	69
11	<i>t</i> -BuONO	3.0	CH ₂ Cl ₂	67
12	<i>t</i> -BuONO	4.5	CH ₂ Cl ₂	66

^[a] Aniline (1 mmol), diazotizing agent (1.2 mmol) and SiF₄ were agitated in the solvent (3 ml) at room temp. for 1 h. After the solvent was evaporated, the reaction mixture was heated at 130–140 °C for 1 h. – ^[b] Yield was determined by gas chromatography.

The deaminative fluorination of various aromatic amines was examined. The results are summarized in Table 2. Substituted anilines and 1-naphthylamine gave the corresponding fluoroarenes in reasonable yields (entry 1–12), which are comparable to that of the Schieman reaction (method A in Table 2). However, diazotization reaction did not proceed in the case of 2-aminopyridine (entry 13).

It should be noted that the reaction is applicable to *p*-cyanoaniline, which has cyano group sensitive to HF, be-

Table 2. Deaminative fluorination of aromatic amines^[a]

Entry	Aromatic amine	Yield ^[b] of fluorobenzene [%]	Yield by the other method A ^[c] [%]	B ^[d] [%]
1	C ₆ H ₅ -NH ₂	60 (69) ^[e]	51–90	99
2	<i>o</i> -CH ₃ -C ₆ H ₄ -NH ₂	69	45–65	99
3	<i>m</i> -CH ₃ -C ₆ H ₄ -NH ₂	60	69–87	98
4	<i>p</i> -CH ₃ -C ₆ H ₄ -NH ₂	64	70	98
5	<i>o</i> -Cl-C ₆ H ₄ -NH ₂	40	6–65	72
6	<i>m</i> -Cl-C ₆ H ₄ -NH ₂	50	83	98
7	<i>p</i> -Cl-C ₆ H ₄ -NH ₂	60	63	92
8	<i>p</i> -CH ₃ OCO-C ₆ H ₄ -NH ₂	61	–	–
9	<i>p</i> -CH ₃ O-C ₆ H ₄ -NH ₂	49	47–73	71
10	<i>p</i> -NC-C ₆ H ₄ -NH ₂	56	–	14
11	<i>p</i> -NO ₂ -C ₆ H ₄ -NH ₂	43	35–58	92
12	1-C ₁₀ H ₇ -NH ₂	35	55–61	–
13	2-C ₅ H ₄ N-NH ₂	0	34	94

^[a] Aromatic amine (1 mmol), *t*-butyl nitrite (1.2 mmol) and SiF₄ (1.0–1.5 mmol) were agitated in CH₂Cl₂ (3 ml) at room temp. for 1 h. After the solvent was evaporated, the reaction mixture was heated at 130–140°C (entry 11, 150–160°C) for 1 h. – ^[b] Isolated yield. – ^[c] The yields obtained by the Schiemann reaction (via ArN₂BF₄)^{[7][8]}. – ^[d] The yields obtained by the reaction with pyridine – HF^{[8][12][13]}. – ^[e] Yield determined by gas chromatography.

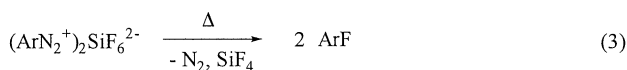
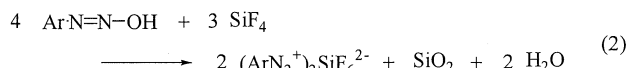
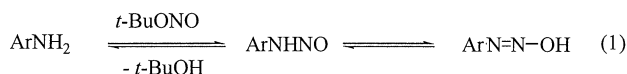
cause the reaction condition is much less-acidic. Although the deaminative fluorination using pyridine–HF (method B in Table 2) affords high yields of fluoroarenes from almost all substrates, in the case of *p*-cyanoaniline, *p*-fluorobenzonitrile was obtained only in 14% yield^{[12][13]}. On the other hand, 56% yield of *p*-fluorobenzonitrile was obtained by the method using SiF₄ (entry 10 in Table 2).

Concerning the reaction intermediate, the product obtained by the reaction of aniline with *t*-butyl nitrite and SiF₄ showed IR absorption at 2290 cm^{–1}, which is assigned to N–N stretching of benzenediazonium ion^[14]. From ¹⁹F-NMR spectrum of the product, broad ¹⁹F signal was observed at –134.5 ppm ([D₆]DMSO as solvent, CFCl₃ as internal standard). These result suggests that the intermediate of this reaction is benzenediazonium hexafluorosilicate [(PhN₂⁺)₂SiF₆^{2–}], which was identified by comparison of the spectral data with those of the authentic sample prepared by a literature method^[15].

It is well-known that alkyl nitrite is a mild reagent for diazotization in organic solvent, and the mechanism of diazotization is considered that nucleophilic attack of amine on the nitroso nitrogen atom affords *N*-nitrosoamine, which isomerizes to diazohydroxide^{[16][17][18]} (Scheme 2, equation 1). If the Brønsted acid exists, the diazohydroxide is protonated and forms diazonium ion. But in this reaction, it is assumed that the arenediazohydroxide reacts with SiF₄, which is a weak Lewis acid, to form the intermediate [(PhN₂⁺)₂SiF₆^{2–}] (Scheme 2, equation 2). The product fluoroarene would be obtained by the decomposition of (PhN₂⁺)₂SiF₆^{2–} as usual Schiemann reaction^[15] (Scheme 2, equation 3). From the stoichiometry of this hypothesis, 0.75 mol of SiF₄ is necessary for 1 mol of the substrate. The result that 1 mol of SiF₄ to 1 mol of the substrate was necessary to obtain a maximum yield (Table 1, entry 10) is reasonable in consideration of the effectiveness of the reaction.

In conclusion, we have demonstrated that the diazotization of aniline derivatives proceeds with SiF₄ and *t*-butyl nitrite, and the corresponding fluoroarenes are obtained by following decomposition of the diazonium salts. This is a first report of the deaminative fluorination using SiF₄ as a sole fluorine source.

Scheme 2. Possible reaction route



Experimental Section

General: All of the reagents are commercially available. All of the organic reagents and solvents were purified prior to use. SiF₄ was used without purification. – IR: Japan Spectroscopic FT-IR 8900. – NMR: JEOL JNM-EX270 (270 MHz). For ¹H NMR, CDCl₃ as solvent, TMS as internal standard; for ¹⁹F NMR, CDCl₃ as solvent, CFCl₃ as internal standard.

Typical Experimental Procedure for Deaminative Fluorination: Aniline derivative (1.0 mmol) dissolved in 3 ml of dichloromethane was placed in a stainless-steel reactor equipped with a stop valve. SiF₄ (1.0–1.5 mmol) and *t*-butyl nitrite (1.2 mmol) were introduced into the reactor at –196°C from a vacuum line. The reactor warmed up to ambient temp. and shaken vigorously for 1 h. After the solvent was evaporated, the reactor was heated to 130–140°C (150–160°C for *p*-nitroaniline) for 1 h. The crude product was transferred from the reactor using a vacuum line system and purified by bulb-to-bulb or trap-to-trap distillation^[19] to give the product. The products were identified by comparison of their IR, ¹H-NMR, and ¹⁹F-NMR spectra with those of authentic samples.

Attempt for Identification of the Intermediate: A solution of 290 mg of aniline (3.1 mmol) dissolved in 6 ml of dichloromethane was placed in a stainless-steel reactor equipped with a stop valve. SiF₄ (3.8 mmol) and *t*-butyl nitrite (4.7 mmol) were introduced into the reactor at –196°C from a vacuum line. The reactor warmed up to ambient temperature and shaken vigorously for 1 h. The solvent was evaporated to obtain the crude product, and its IR, ¹H-NMR, and ¹⁹F-NMR spectra was measured. – IR (*n*-dodecane disp.): $\tilde{\nu}$ = 2290 cm^{–1} (NN str.). – ¹H NMR ([D₆]DMSO): δ = 7.95–8.00 (m, 2 H, aromatic H), 8.23–8.29 (m, 2 H, aromatic H), 8.66–8.69 (m, 2 H, aromatic H), small signals, which would be due to by-products, were observed from 6.7 to 7.8 ppm. – ¹⁹F NMR ([D₆]DMSO): δ = –134.5 (br).

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