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

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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 fluorodediazoniation affords fluoroarenes in good yields.

Silicon tetrafluoride (SiF_4) 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 SiF_4 to organic synthesis, although its reactivity to organic compounds were somewhat investigated[2], there had been very few reports about the utility of SiF_4 as a fluorine source, namely ring-opening of epoxides and halofluorination 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 (KHF_2) and SiF_4 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 SiF_4 as a sole fluorine source to deaminative fluorination of aromatic amines (Scheme 1).

Scheme 1. Deaminative fluorination of aromatic amines

$$\text{Ar-NH}_2 \xrightarrow{SiF_4,\quad RONO} \xrightarrow{\Delta} \text{Ar-F}$$

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 KHF_2 and SiF_4 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 SiF_4 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 diazotizating 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 SiF_4, the yields were almost same when the amount of SiF_4 was more than 1.0 molar equivalent to the substrate, although the yield diminished when less than 1.0 molar equivalent of SiF_4 was used (entry 8−12).

Table 1. Deaminative fluorination of aniline[a]

Entry	Diazotizating agent	Amount of SiF_4 (mmol)	Solvent	Yield[b] [%]
1	*t*-BuONO	1.5	CH_2Cl_2	69
2	$NaNO_2$	1.5	CH_2Cl_2	0
3	*n*-BuONO	1.5	CH_2Cl_2	2
4	*t*-BuONO	1.5	Et_2O	0
5	*t*-BuONO	1.5	*n*-hexane	0
6	*t*-BuONO	1.5	C_6H_6	0
7	*t*-BuONO	1.5	CH_3CN	34
8	*t*-BuONO	0.5	CH_2Cl_2	< 1
9	*t*-BuONO	0.75	CH_2Cl_2	54
10	*t*-BuONO	1.0	CH_2Cl_2	69
11	*t*-BuONO	3.0	CH_2Cl_2	67
12	*t*-BuONO	4.5	CH_2Cl_2	66

[a] Aniline (1 mmol), diazotizating agent (1.2 mmol) and SiF_4 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-naphtylamine gave the corresponding fluoroarenes in reasonable yields (entry 1−12), which are comparable to that of the Schiemann 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-

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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_6H_5-NH_2	60 (69)[e]	51–90	99
2	*o*-CH_3-C_6H_4-NH_2	69	45–65	99
3	*m*-CH_3-C_6H_4-NH_2	60	69–87	98
4	*p*-CH_3-C_6H_4-NH_2	64	70	98
5	*o*-Cl-C_6H_4-NH_2	40	6–65	72
6	*m*-Cl-C_6H_4-NH_2	50	83	98
7	*p*-Cl-C_6H_4-NH_2	60	63	92
8	*p*-CH_3OCO-C_6H_4-NH_2	61	–	–
9	*p*-CH_3O-C_6H_4-NH_2	49	47–73	71
10	*p*-NC-C_6H_4-NH_2	56	–	14
11	*p*-NO_2-C_6H_4-NH_2	43	35–58	92
12	1-$C_{10}H_7$-NH_2	35	55–61	–
13	2-C_5H_4N-NH_2	0	34	94

[a] Aromatic amine (1 mmol), *t*-butyl nitrite (1.2 mmol) and SiF_4 (1.0–1.5 mmol) were agitated in CH_2Cl_2 (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 ArN_2BF_4)[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 Table2) 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 SiF_4 (entry 10 in Table 2).

Concerning the reaction intermediate, the product obtained by the reaction of aniline with *t*-butyl nitrite and SiF_4 showed IR absorption at 2290 cm^{-1}, which is assigned to N–N stretching of benzenediazonium ion[14]. From ^{19}F-NMR spectrum of the product, broad ^{19}F signal was observed at –134.5 ppm ([D$_6$]DMSO as solvent, $CFCl_3$ as internal standard). These result suggests that the intermediate of this reaction is benzenediazonium hexafluorosilicate [$(PhN_2^+)_2SiF_6^{2-}$], 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 SiF_4, which is a week Lewis acid, to form the intermediate [$(PhN_2^+)_2SiF_6^{2-}$] (Scheme 2, equation 2). The product fluoroarene would be obtained by the decomposition of $(PhN_2^+)_2SiF_6^{2-}$ as usual Schiemann reaction[15] (Scheme 2, equation 3). From the stoicheiometry of this hypothesis, 0.75 mol of SiF_4 is necessary for 1 mol of the substrate. The result that 1 mol of SiF_4 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 SiF_4 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 SiF_4 as a sole fluorine source.

Scheme 2. Possible reaction route

$$\mathrm{ArNH_2} \xrightleftharpoons[-\,t\text{-BuOH}]{t\text{-BuONO}} \mathrm{ArNHNO} \rightleftharpoons \mathrm{ArN{=}N{-}OH} \qquad (1)$$

$$4\ \mathrm{ArN{=}N{-}OH} + 3\ \mathrm{SiF_4} \longrightarrow 2\ (\mathrm{ArN_2^+})_2\mathrm{SiF_6^{2-}} + \mathrm{SiO_2} + 2\ \mathrm{H_2O} \qquad (2)$$

$$(\mathrm{ArN_2^+})_2\mathrm{SiF_6^{2-}} \xrightarrow[-\,\mathrm{N_2},\ \mathrm{SiF_4}]{\Delta} 2\ \mathrm{ArF} \qquad (3)$$

Experimental Section

General: All of the reagents are commercially available. All of the organic reagents and solvents were purified prior to use. SiF_4 was used without purification. – IR: Japan Spectroscopic FT-IR 8900. – NMR: JEOL JNM-EX270 (270 MHz). For ^1H NMR, $CDCl_3$ as solvent, TMS as internal standard; for ^{19}F NMR, $CDCl_3$ as solvent, $CFCl_3$ 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. SiF_4 (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 ^{19}F-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. SiF_4 (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 ^{19}F-NMR spectra was measured. – IR (*n*-dodecane disp.): $\tilde{\nu}$ = 2290 cm^{-1} (NN str.). – ^1H NMR ([D$_6$]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. – ^{19}F NMR ([D$_6$]DMSO): δ = –134.5 (br).

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