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A New Approach to Polyfluoroalkyl Imidoyl Iodide

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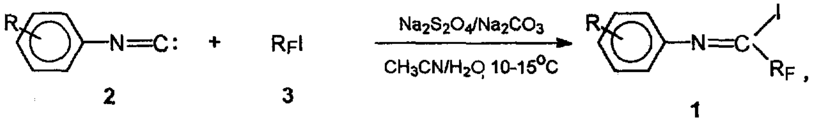
Abstracts: Polyfluoroalkyl imidoyl iodide were prepared by reaction of polyfluoroalkyl iodide with N-aryl isocyanide in the presence of sulfinatodehalogenation reagent ($Na_2S_2O_4/Na_2CO_3$).

Recently much attention has been paid to the development of new methodologies for the syntheses of many kinds of fluorine-containing building blocks, due in part to the unique biological and medicinal properties imparted by fluorine substitution.[1] Among them, the fluorinated imidoyl halides, especially the N-aryl trifluoroacetmidoyl halide, have considerable value toward the syntheses of fluoroalkyl or trifluoromethyl substituted heteroaromatic compounds.[2] This building block can be regarded as the corresponding trifluoroacetimidoyl carbocations, carbanions or radical intermediates.[2,3]

However, the syntheses of trifluoromethylated or per(poly)fluoroalkylated imidoyl halides have been quite limited so far.[4] During our investigations on the radical addition of polyfluoroalkyl halide to double or triple bond by sulfinatodehalogenation reagent ($Na_2S_2O_4/NaHCO_3$ or Na_2CO_3), it was found that the polyfluoroalkyl radical can easily reacted with alkene, alkyne, aromatic ring to give versatile fluorinated organic compounds or intermediates for further chemical conversions.[5] In addition, it has been known that radicals add to isocyanide to form imidoyl radicals,[6,7] or α-stannoimidoyl radicals[8] which have been demonstrated to have strong synthetic potentials for inter- and intramolecular carbon-carbon bond formation. This situation prompts us to report herein our work on the synthesis of the title compounds by reaction of R_FI with N-aryl isocyanide in a direct and mild condition.

Scheme 1



3a $R_F=Cl(CF_2)_2$
3b $R_F=Cl(CF_2)_4$
3c $R_F=CF_3$

Using the $Na_2S_2O_4/Na_2CO_3$ reagent system (Scheme 1), R_FI (**2**) can easily generate $R_F^{\cdot}$ which then reacted with the isocyanide at 10-15°C during 40-60 minutes to provide the corresponding imidoyl iodide. The yields seemed to be affected slightly by the electronic effects of substituents on the aromatic nucleus in the cases examined so far (Table 1). Aryl isocyanides with o- or p-substituted electron donating group gave high yields. A volumn ratio 4:3 of CH_3CN and H_2O gave satisfactory results. However, when the reaction was carried out with $NaHCO_3$ instead of Na_2CO_3, the reaction took a much longer time with the decomposition of isocyanide. Lower temperature prolonged the reaction time and a higher temperature resulted in the production of R_FSO_2Na. The optimal reaction temperature is 10-15°C. In this condition, the reaction can be run on 30mmol

Table 1. Radical Addition of R_FI to N-aryl Isocyanide

entry	R	R_F	time[a]	Product/Yields[b]	entry	R	R_F	time	Product/Yields[b]
1	p-CH_3O (**2a**)	**3a**	40	**1aa**/92	9	p-Cl (**2e**)	**3a**	45	**1ea**/61
2	p-CH_3O (**2a**)	**3b**	40	**1ab** /91	10	p-Cl (**2e**)	**3b**	45	**1eb**/67
3	p-CH_3 (**2b**)	**3a**	40	**1ba**/86	11	o-Cl (**2f**)	**3a**	45	**1fa**/68
4	p-CH_3 (**2b**)	**3b**	40	**1bb**/93	12	o-Cl (**2f**)	**3b**	45	**1fb**/73
5	p-I (**2c**)	**3a**	45	**1ca**/74	13	o-Br (**2g**)	**3a**	45	**1ga**/72
6	p-I (**2c**)	**3b**	45	**1cb**/78	14	o-Br (**2g**)	**3b**	45	**1gb**/67
7	o-I (**2d**)	**3a**	45	**1da**/72	15	p-CH_3O (**2a**)	**3c**	60	**1ac**/35
8	o-I (**2d**)	**3b**	45	**1db**/83					

a: reaction time (minutes); b: isolated yields(%) based on compound 2.

scale. In the case of CF_3I [9] the yield of trifluoromethylated imidoyl iodide was not satisfactory. Furthermore, the polyfluoroalkylated imidoyl iodide is more stable than the trifluoromethyl analog at room temperature. Thus, compound **1aa** or **1ab** can be stored in a sealed bottle at room temperature without deterioration whereas compound **1ac** should be stored in refrigerator.

Representative Synthetic Procedure:

N-aryl isocyanide were prepared according to the literature.[10a] A solution of **2a** (133mg, 1.0mmol) and **3a** (289mg, 1.1mmol) in CH_3CN (2ml) and H_2O (1.5ml) was cooled to 10-15°C and treated with a mixture of powdered $Na_2S_2O_4$ (230mg, 1.32mmol) and Na_2CO_3 (140mg, 1.32mmol) with stirring. Five minutes later, the color of the reaction mixture turned to brown. After 40min, the mixture was quenched with 20ml H_2O and extracted with ethyl ether (20ml×3). The organic layer was washed with brine and then dried (Na_2SO_4) and concentrated. The crude product was purified by flash column chromatography[10b] (silica gel, petroleum ether elution(b.p.60-90°C)) to give **1aa** (364mg, 92%) as a pale yellow oil. Anal. calcd. for $C_{10}H_7F_4ClINO$: C 30.37, H 1.78, N 3.54, F 19.21%, found: C 30.20, H 1.66, N 3.59, F 19.66%; ^{1}H NMR(90MHz, $CDCl_3$) δ 6.97 (s, 4H, Ar-H), 3.83(s, 3H, CH_3O); ^{19}F NMR(56.4MHz, $CDCl_3$, $CFCl_3$ as the external standard[10c]) δ 66.3(s, 2F, CF_2Cl), 103.1(s, 2F, CF_2); IR (ν cm-1) 2840, 1675-1695, 1600, 12504, 1300, 1250, 1230, 1175-1150, 1099; MS 395(M^+, 1.66), 360(M^+-Cl, 4.50), 268(M^+-I, 100), 107(CH_3OAr, 18.83).

In conclusion, we have described a novel reaction between R_FI and N-aryl isocyanide in the presence of $Na_2S_2O_4/Na_2CO_3$ reagent system. It not only gives a new synthetic method of fluorinated imidoyl iodide which can be a useful building block in organic synthesis but also broadens the scope of the sulfinatodehalogenation.

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