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A mild method for halofluorination of alkenes with ionic liquid EMIMF(HF)$_{2.3}$

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Abstract

Halofluorination of alkene in the presence of *N*-halosuccinimide and ionic liquid, 3-ethyl-1-methyl-imidazorium oligo hydrogen fluoride (EMIMF(HF)$_{2.3}$), as a HF source was demonstrated. Various alkenes were converted into β-halo organofluorides in good yields and with high regioselectivity.

Keywords: Iodofluorination of alkene; Bromofluorination of alkene; Ionic liquid; Hydrogen fluoride

1. Introduction

Halofluorination of unsaturated hydrocarbon has been a useful method to incorporate fluorine atom, and the obtained β-halo subunit acquires for further reaction to gain various organofluoro compounds [1,2]. To prepare it, alkenes are treated with halonium ion and fluoride ion. However, fluoride ion source in these procedures, elemental fluorine [3,4], hydrogen fluoride [5,6], HF-pyridine (Olah's reagent) [7,8] and Et_3N-3HF [9] contain difficulty to handle in some extent. In this situation, ionic liquid containing fluoride ion may have a possibility to solve these difficulty. 3-Ethyl-1-methyl-imidazorium oligo hydrogen fluoride (EMIMF(HF)$_{2.3}$), ionic liquid, is available in air with easy and safety handle due to its non-volatility and poor solubility to organic solvent. Herein, we wish report halofluorination of alkenes with combination of halosuccinimide and this ionic liquid as a fluorinating reagent.

2. Results and discussion

EMIMF(HF)$_{2.3}$ was synthesized by a direct reaction of 1-ethyl-3-methyl-imidazolium chloride and anhydrous hydrogen fluoride [10]. This ionic liquid is stable against moisture in air. It consists of 3-ethyl-1-methyl-imidazorium cation and F(HF)$_{2.3}$ anion, which a rapid exchange of HF between H_2F_3 and H_3F_4 occurs [10]. So, we expected that this HF could be available as fluoride ion source (Fig. 1).

Reactions were carried out in polypropylene toll tube that is easy for decantation in work-up process. To a mixture of substrate in CH_2Cl_2 and ionic liquid, *N*-iodosuccinimide (NIS) was added in several portions. The reaction mixture gradually turned to be clear and yellow. Extraction of product is only to add hexane to the reaction mixture. The resulting mixture became biphase. Decantation of upper phase gave a hexane solution of the produced β-halofluoride. After the solution was passed through short silica-gel column, it was concentrated under reduced pressure (Scheme 1).

Results of iodofluorination of alkenes are summarized in Table 1. NIS required two equivalent for substrate otherwise

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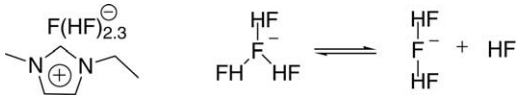
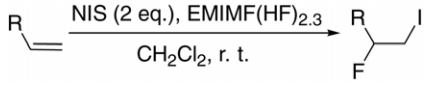
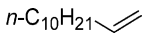
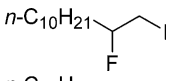
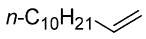
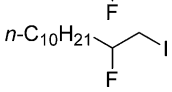
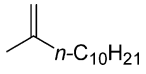
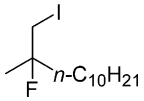
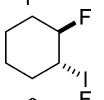
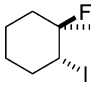
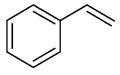
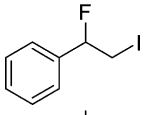
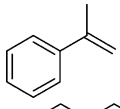
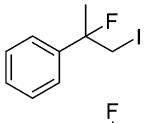
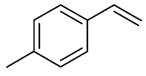
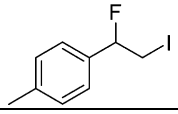


Fig. 1. EMIMF(HF)$_{2.3}$.



Scheme 1.

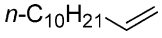
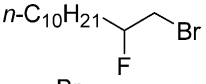
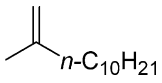
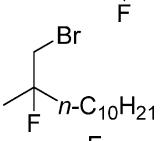
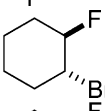
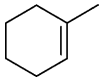
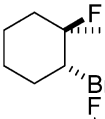
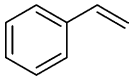
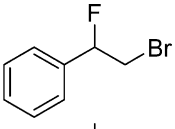
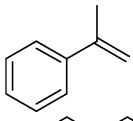
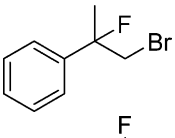
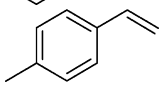
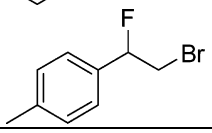
Table 1
Iodofluorination of alkenes

Entry	Alkene	Time (h)	Product	Yield (%)
1		3		80
2		36		64[a]
3		1		91
4		1		95
5		1		98
6		1		70
7		1		88
8		1		78

[a] N1S of 1 mmol was used and 30% of starting material was remained.

starting material was remained (Table 1, entries 1 and 2). The iodofluorination products of various alkenes, aliphatic, cyclic, and aryl alkenes, were gained in good yields and with high regioselectivity. The stereochemistry of this addition is *anti*-manner (entries 3 and 4). When 1-fluoro-2-iodo-1-phenylpropane, prepared from (*E*)-1-phenylpropene, was treated with DBU at room temperature, dehydroiodination occurred to give (*Z*)-1-fluoro-1-phenylpropene stereospecifically (Scheme 2) as reported by Schlosser [11,12].

Table 2
Bromofluorination of alkenes

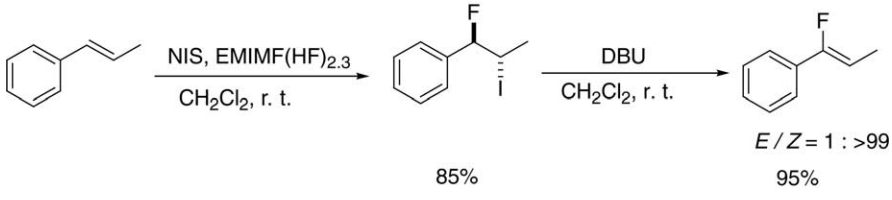
Entry	Alkene	Time (h)	Product	Yield (%)
1		3		86
2		1		90
3		1		90
4		1		95
5		1		81
6		1		87
7		1		93

Bromofluorination of alkenes were also occurred under the same conditions using *N*-bromosuccinimide (NBS) instead of NIS. Results are summarized in Table 2. Bromo fluoride compounds were gained in the same or higher yield than iodo fluoride compounds due to their stability. Chlorofluorination was also examined by *N*-chlorosuccinimide, but it resulted in low yields in spite of longer reaction time (Scheme 3).

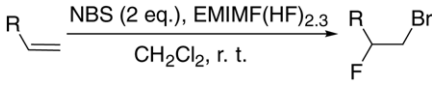
In summary, we demonstrated halofluorination of alkenes with mild and safe fluorinating reagent EMIMF(HF)$_{2.3}$ under open air.

3. Experimental

Reagents were purchased from Wako Chemical Inc. or Tokyo Kasei, and used without further purification. Reactions



Scheme 2.



Scheme 3.

were monitored by thin-layer chromatography using 25 mm E. Merck silica-gel plates (silica-gel F_{254}). Silica-gel was purchased from Kanto Chemical Co. The polypropylene tube used was a centrifuge tube (15 ml) with a screw cap, and was purchased from Corning. NMR spectra were recorded on a Varian Gemini 300 or Mercury 2000 in $CDCl_3$. $EMIMF(HF)_{2.3}$ was prepared followed by the literature [10].

3.1. General procedure for halofluorination

In a 15-ml polypropylene tube, CH_2Cl_2 (500 μl) solution of alkene (1 mmol) and $EMIMF(HF)_{2.3}$ (600 μl) were placed and stirred with magnetic stirrer vigorously. To this reaction mixture, *N*-halosuccinimide (2 mmol) was added in several portions at room temperature. When the reaction finished, 1 ml of hexane or ether was added and the upper layer was collected by decantation three times. The organic layer was passed through short silica-gel column, and evaporated.

3.2. 2-Fluoro-1-iodo-dodecane

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.41 (ddt, J = 48.0, 10.8, 1.5 Hz, 1H), 3.31 (ddd, J = 20.1, 5.7, 2.1 Hz, 2H), 1.80–1.65 (m, 2H), 1.45–1.20 (m, 16H), and 0.88 (t, J = 6.9 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ 170.6 (m).

3.3. 1-Fluoro-2-iodo-cyclohexane

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.52 (ddt, J = 47.7, 8.7, 4.5 Hz, 1H), 4.16–4.06 (m, 1H), 2.44–2.30 (m, 1H), 2.28–2.13 (m, 1H), 2.02–1.78 (m, 2H), 1.66–1.54 (m, 2H), and 1.50–1.24(m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$): δ 159.5 (m).

3.4. (1-Fluoro-2-iodo-ethyl)-benzene

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50–7.30 (m, 5H), 5.53 (ddd, J = 46.5, 7.2, 4.8 Hz, 1H), and 3.55–3.41 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$): δ 166.4 (ddd, J = 46.5, 23.7, 17.8 Hz).

3.5. 1-(1-Fluoro-2-iodo-ethyl)-4-methyl-benzene

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28–7.15 (m, 4H), 5.52 (ddd, J = 45.3, 18.6, 6.3 Hz, 1H), 3.55–3.40 (m, 2H), and 2.37 (s, 3H).

3.6. Erythro-(1-fluoro-2-iodo-propyl)-benzene

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39–7.13 (m, 5H), 5.53 (dd, J = 46.5, 6.0 Hz, 1H), and 4.49–4.34 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$): δ 172.3 (dd, J = 46.5, 17.2 Hz).

3.7. (E)-1-Fluoro-1-phenyl-1-propene

To a solution of (1-fluoro-2-iodo-propyl)-benzene (0.5 mmol) in CH_2Cl_2 (5 ml) was added DBU (0.15 g, 1 mmol) at room temperature. The reaction mixture was stirred for 12 h at ambient temperature, and then quenched with sat. NH_4Cl aq. and extracted with hexane three times. The combined organic layer was dried over Na_2SO_4, and evaporated. The crude was purified with silica-gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50–7.35 (m, 5H), 5.47 (dq, J = 22.5, 7.5 Hz, 1H), and 1.80 (dd, J = 7.5, 2.7 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ 102.6 (dq, J = 22.5, 2.7 Hz).

3.8. 1-Bromo-2-fluoro-dodecane

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.62 (dddt, J = 48.6, 7.5, 5.4, 5.4 Hz, 1H), 3.51 (ddd, J = 19.8, 10.8, 5.4 Hz, 2H), 1.77–1.64 (m, 2H), 1.49–1.26 (m, 16H), and 0.88 (t, J = 6.8 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ 178.0 (dddt, J = 48.6, 27.0, 19.8, 19.8 MHz).

3.9. 2-Bromo-1-fluoro-1-phenyl-benzene

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51–7.35 (m, 5H), 5.50 (ddd, J = 46.8, 7.2, 4.2 Hz, 1H), and 3.64–3.43 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$): δ 174.1 (ddd, J = 46.8, 23.7, 16.5 MHz).

Acknowledgements

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