Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Fluorine Chemistry 125 (2004) 455–458
JOURNAL OF FLUORINE CHEMISTRY
www.elsevier.com/locate/jfluchem

Halofluorination of alkenes with ionic liquid EMIMF(HF)$_{2.3}$

Hideaki Yoshino[a], Seijiro Matsubara[a,*], Koichiro Oshima[a], Kazuhiko Matsumoto[b], Rika Hagiwara[b], Yasuhiko Ito[b]

[a]*Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Kyoutodaigaku-Katsura, Nishikyo, Kyoto 615-8510, Japan*
[b]*Department of Fundamental Energy Science, Graduate School of Energy Science, Kyoto University, Yoshida hon-machi, Sakyo, Kyoto 606-8501, Japan*

Received 25 August 2003; received in revised form 25 November 2003; accepted 29 November 2003

Abstract

Halofluorination of alkene by means of *N*-halosuccinimide and ionic liquid, 1-ethyl-3-methylimidazorium oligo hydrogenfluoride (EMIMF(HF)$_{2.3}$), was demonstrated. Various alkenes were converted into β-halo organofluorides in good yields after non-aqueous work-up.

Keywords: Iodofluorination; Bromofluorination; Ionic liquid; Hydrogen fluoride

1. Introduction

Halofluorination of alkenes has been a useful method to incorporate fluorine atom into organic molecules, and the obtained β-halo subunit is available for further reaction to obtain various organofluoro compounds [1,2]. To prepare *vic*-halofluoroalkanes, alkenes are reacted with halonium ion and fluoride ion. As fluoride ion sources in these procedures, elemental fluorine [3], hydrogen fluoride [4,5], HF-pyridine (Olah's reagent) [6,7], Et_3N-3HF [8], silver fluoride [9], potassium fluoride-poly(hydrogen fluoride) [10], and silicon tetrafluoride [11] have been used. In these procedures, the difficulties to handle these reagents should be taken care because of their hazardous property and the occurrence of HF at the aqueous work-up could not be avoided. Recently, ionic liquid has been paid much attention because of the easiness in handling and the possibility of non-aqueous work-up especially in the field of green chemistry and combinatorial chemistry [12]. 1-Ethyl-3-methylimidazorium oligo hydrogen fluoride (EMIMF(HF)$_{2.3}$), ionic liquid, which is stable in air and moisture, might be used as fluoride ion source ionic liquid. Herein, we wish to report halofluorination of alkenes with combination of *N*-halosuccinimide and the ionic liquid.

2. Results and discussion

EMIMF(HF)$_{2.3}$ was synthesized by a direct reaction of 1-ethyl-3-methylimidazolium chloride and anhydrous hydrogen fluoride according to the reported procedure [13]. This ionic liquid is stable against moisture and air. It consists of 1-ethyl-3-methylimidazorium cation and F(HF)$_{2.3}$ anion, in which a rapid exchange of HF between H_2F_3 and H_3F_4 occurs [13] (Fig. 1).

Reactions were carried out in polypropylene tall tubes that are easy to handle for decantation in work-up process. To a mixture of substrate dissolved 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. When the reaction was finished, hexane was added 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 a short silica-gel column, it was concentrated under reduced pressure (Scheme 1).

Results of iodofluorination of alkenes are summarized in Table 1. The iodofluorination products of various alkenes, aliphatic, cyclic, and aryl alkenes were obtained in good yields and with high regioselectivity. As shown in entries 3 and 4, the reaction proceeded with *anti*-manner. When 1-fluoro-2-iodo-1-phenylpropane, prepared from (*E*)-1-phenylpropene, was treated with DBU at room temperature, dehydroiodination occurred to give (*E*)-1-fluoro-

* Corresponding author. Tel.: +81-75-383-2441; fax: +81-75-383-2438.
E-mail address: matsubar@mc.kyoto-u.ac.jp (S. Matsubara).

0022-1139/$ – see front matter © 2003 Elsevier B.V. All rights reserved.
doi:10.1016/j.jfluchem.2003.11.015

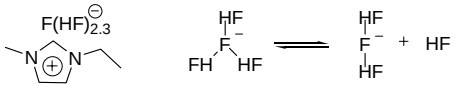
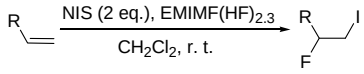


Fig. 1. EMIMF$(HF)_{2.3}$.



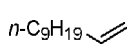
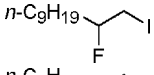
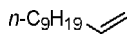
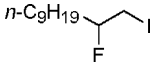
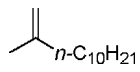
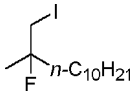
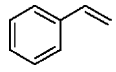
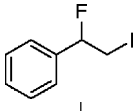
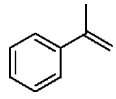
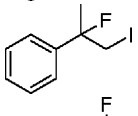
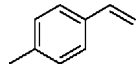
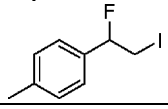
Scheme 1.

1-phenylpropene stereospecifically (Scheme 2) as reported by Schlosser [14,15].

Bromofluorination of olefines also proceeded under the same conditions using *N*-bromosuccinimide (NBS) instead of NIS. Results are summarized in Table 2. *vic*-Bromofluoroalkanes were also obtained in good yields. Chlorofluorination was also examined by *N*-chlorosuccinimide, but resulted in low yields in spite of longer reaction time (Scheme 3).

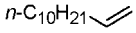
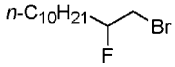
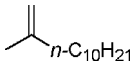
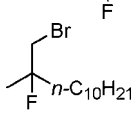
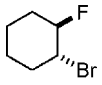
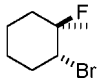
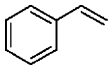
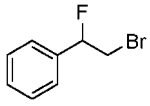
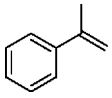
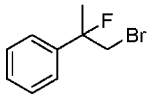
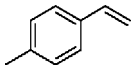
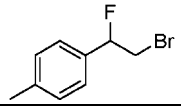
In summary, we demonstrated halofluorination of alkenes with mild and safe fluorinating reagent EMIMF$(HF)_{2.3}$ which makes the non-aqueous work-up possible.

Table 1
Iodofluorination of alkenes

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

[a] 1-Fluoro-2-iodo-undecane was also obtained in 2% yield.
[b] 1 mmol of NIS was used. Thirty percent of starting material was remained.

Table 2
Bromofluorination of alkenes

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

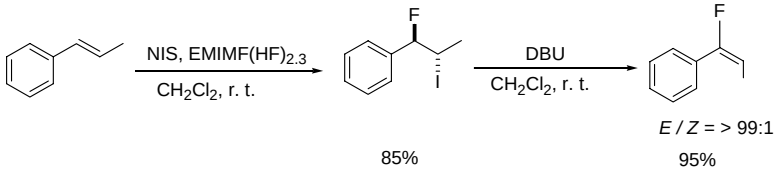
[a] 1-Fluoro-2-bromo-decane was also obtained in 9% yield.

3. Experimental

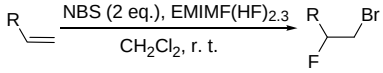
Reagents were purchased from Wako Chemical, Inc. or Tokyo Kasei, and used without further purification. Reactions were monitored by thin-layer chromatography using 25 mm *E*. Merck silica-gel plates (Silica Gel F_{254}). Silica-gel was purchased from Kanto Chemical Co. The polypropylene tube used was a centrifuge tube (15 ml) with a screw cap, and is available from Corning. NMR spectra were recorded on a Varian Gemini 300 or Mercury 2000 in $CDCl_3$. EMIMF$(HF)_{2.3}$ was prepared according to the literature [13].

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, hexane (1 ml) was added and the whole was stirred vigorously. The stirring was stopped, the mixture was separated into two phases. The upper layer was collected by decantation. This extraction with hexane was repeated twice more. The combined hexane layers were passed through a short silica-gel column (1 cm) to obtain crude product. The crude product was purified by a short silica-gel column chromatography. Yield was determined by ^{19}F NMR in comparison with internal standard.



Scheme 2.



Scheme 3.

3.2. 2-Fluoro-1-iodo-undecane

^{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), 0.88 (t, $J = 6.9$ Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −170.6 (m).

3.3. 2-Fluoro-1-iodo-2-methyl-dodecane

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.34 (d, $J = 16.8$ Hz, 2H), 1.83–1.72 (m, 2H), 1.49 (d, $J = 21.0$ Hz, 3H), 1.40–1.20 (m, 16H), 0.88 (t, $J = 6.9$ Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −140.0 (m).

3.4. 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), 1.50–1.24 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −159.5 (m).

3.5. 1-Fluoro-2-iodo-1-methyl-cyclohexane

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.37 (dt, $J = 8.1$, 4.2 Hz, 1H), 2.30–2.08 (m, 2H), 2.00–1.87 (m, 1H), 1.82–1.62 (m, 3H), 1.56 (d, $J = 22.2$ Hz, 3H), 1.54–1.40 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −132.4 (m).

3.6. (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), 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).

3.7. (1-Fluoro-2-iodo-1-methyl-ethyl)-benzene

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50–7.30 (m, 5H), 3.59 (d, $J = 20.4$ Hz, 2H), 1.86 (d, $J = 21.6$ Hz, 3H). ^{19}F NMR (282 MHz, CDCl3): δ −142.4 (tq, $J = 21.6$, 20.4 Hz).

3.8. 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), 2.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.3, 135.1 (d, $J = 20.5$ Hz), 129.6, 125.8 (d, $J = 6.2$ Hz), 93.4 (d, $J = 175.5$ Hz), 21.7, 7.9 (d, $J = 28.8$ Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ −164.6 (ddd, $J = 45.4$, 23.7, 15.8 Hz). Anal. Calcd for C9H10FI: C, 40.93; H, 3.82. Found: C, 40.66; H, 3.69.

3.9. 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), 4.49–4.34 (m, 2H) 1.91 (d, $J = 6.9$ Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −172.3 (dd, $J = 46.5$, 17.2 Hz).

3.10. (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_4Claq and extracted with hexane three times. The combined organic layers were dried over Na_2SO_4, and evaporated. The crude was purified with a 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), 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).

3.11. 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), 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 Hz).

3.12. 1-Bromo-2-fluoro-2-methyl-dodecane

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.46 (d, $J = 15.9$ Hz, 2H), 1.80–1.71 (m, 2H), 1.46 (d, $J = 21.3$ Hz, 3H), 1.39-1.26 (m, 16H), 0.88 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 95.0 (d, $J = 171.5$ Hz), 38.3 (dd, $J = 41.2$, 25.6 Hz), 32.0, 29.8, 29.7, 29.6, 29.5, 29.4, 23.6, 23.6, 23.5, 23.4, 23.3, 22.8.

^{19}F NMR (282 MHz, $CDCl_3$): δ −144.9 (m). Anal. Calcd for C13H26FBr: C, 55.52; H, 9.32. Found: C, 55.59; H, 9.13.

3.13. 1-Bromo-2-fluoro-cyclohexane

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.48 (ddt, J = 48.0, 8.4, 4.5 Hz, 1H), 4.07–3.97 (m, 1H), 2.35–2.17 (m, 2H), 1.89–1.62 (m, 4H), 1.42–1.31 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −167.4 (dm, J = 48.0 Hz).

3.14. 2-Bromo-1-fluoro-1-methyl-cyclohexane

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.20 (dt, J = 7.2, 3.9 Hz, 1H), 2.35–1.25 (m, 8H), 1.51 (d, J = 22.4, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −137.0 (m).

3.15. 2-Bromo-1-fluoro-1-phenyl-ethane

^{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), 3.64–3.43 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$): δ –174.1 (ddd, J = 46.8, 23.7, 16.5 Hz).

3.16. (2-Bromo-1-fluoro-1-methyl-ethyl)-benzene

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43–7.32 (m, 5H), 3.73–3.60 (m, 2H), 1.84 (d, J = 22.2 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −147.5 (ddq, J = 22.2, 22.2, 18.4 Hz).

3.17. 1-(2-Bromo-1-fluoro-ethyl)-4-methyl-benzene

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38–7.18 (m, 4H), 5.57 (ddd, J = 46.8, 8.1, 4.2 Hz, 1H), 3.75–3.53 (m, 2H), 2.37 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −172.3 (ddd, J = 46.8, 25.9, 18.9 Hz).

Acknowledgements

Financial support by Grant-in-Aid from the Ministry of Education, Science, Sports, and Culture is acknowledged. Financial support by Chugai Pharmaceutical Co. Ltd. is also acknowledged.

References

[1] C.M. Sharts, W.A. Sheppard, Org. React. 21 (1974) 125–406.
[2] T. Hiyama, Organofluorine Compounds, Springer-Verlag, New York, 2000.
[3] S. Rozen, M. Brand, J. Org. Chem. 50 (1985) 3342–3348.
[4] A. Bowers, L.C. Ibáñez, E. Denot, R. Becerra, J. Am. Chem. Soc. 82 (1960) 4001–4007.
[5] A. Bowers, E. Denot, R. Becerra, J. Am. Chem. Soc. 82 (1960) 4007–4012.
[6] G.A. Olah, J.T. Welch, Y.D. Vankar, M. Nojima, I. Kerebe, J.A. Olah, J. Org. Chem. 44 (1979) 3872–3881.
[7] D.Y. Chi, M.R. Kilbourn, J.A. Katzenellenbogen, M.J. Welch, J. Org. Chem. 52 (1987) 658–664.
[8] G. Alvernhe, A. Lawrent, G. Haufe. Synthesis (1987) 562–564.
[9] L.D. Hall, J.F. Manville, Can. J. Chem. 51 (1973) 2902–2913.
[10] M. Tamura, M. Shibakami, A. Sekiya, Synthesis (1995) 515–517.
[11] M. Shimizu, Y. Nakahara, H. Yoshioka, J. Chem. Soc., Chem. Commun. (1989) 1881–1882.
[12] C.C. Tzschucke, C. Markert, W. Bannwarth, S. Roller, A. Hebel, R. Haag, Angew. Chem. Int. Ed. 41 (2002) 3964–4000.
[13] R. Hagiwara, T. Hirashige, T. Tsuda, Y. Ito, J. Electrochem. Soc. 149 (2002) D1–D6.
[14] H. Suga, T. Hamatani, Y. Guggisberg, M. Schlosser, Tetrahedron 46 (1990) 4255–4260.
[15] M. Kuroboshi, T. Hiyama, Bull. Chem. Soc. Jpn. 68 (1995) 1799–1805.