Synthetic Methods and Reactions III[1]. Halofluorination of Alkenes in Poly-Hydrogen Fluoride/Pyridine Solution

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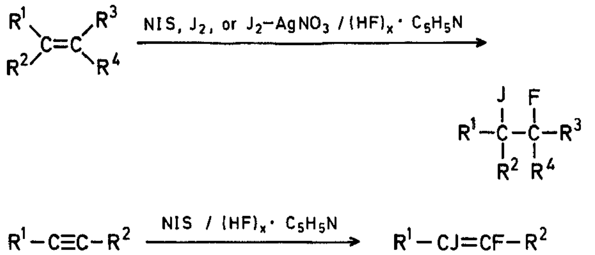
Known halofluorination methods necessitate the use of anhydrous hydrogen fluoride or silver fluoride in connection with *N*-halosuccinimides or related *N*-haloamides to effect the reactions[2].

We wish to report now highly simplified, inexpensive and convenient methods using stable pyridine (trialkylamine)/polyhydrogen fluoride solutions for halofluorination reactions of alkenes and alkynes.

Iodofluorination can be carried out with a solution of iodine in 70% hydrogen fluoride/30% pyridine or with the similar solution of *N*-iodosuccinimide. Data obtained are summarized in Table 1.



$$R^1R^2C{=}CR^3R^4 \xrightarrow{\text{NIS, J}_2\text{, or J}_2\text{–AgNO}_3\text{ / (HF)}_x\cdot \text{C}_5\text{H}_5\text{N}} R^1-\underset{R^2}{\overset{J}{C}}-\underset{R^4}{\overset{F}{C}}-R^3$$

$$R^1-C\equiv C-R^2 \xrightarrow{\text{NIS / (HF)}_x\cdot \text{C}_5\text{H}_5\text{N}} R^1-CJ{=}CF-R^2$$

Table 1. Iodofluorination of Alkenes and Alkynes[a]

Alkenes or alkynes	Products	b.p.,	Yield,	%
		°C	NIS[b]	J_2
Ethene[c]	1-Iodo-2-fluoroethane	96–97°[d]	23	(25[h])
Propene[c]	1-Iodo-2-fluoropropane	50°/20 torr[e]	32	(40[h])
2-Methylpropene[c]	1-Iodo-2-fluoro-2-methylpropane	decomp.[f]	60	35
1-Hexene	1-Iodo-2-fluorohexane	72–75°/16 torr[d]	70	35
3-Hexene	3-Iodo-4-fluorohexane	63–65°/15 torr	65	30
Cyclohexene	1-Iodo-2-fluorocyclohexane	73–75°/10 torr[g]	75	60
Norbornene	7-*anti*-Iodo-2-*exo*-fluoronorbornane	separated by	55	45
	7-*syn*-Iodo-2-*exo*-fluoronorbornane	gaschromatography	30	25
3-Hexyne	3-Iodo-4-fluorohexene-3	62–65°/12 torr	70	(80[h])
Diphenylacetylene	1-Iodo-2-fluoro-1,2-diphenylethene	m.p. 128–130°	90	(90[h])

[a] Alkenes or alkynes (0.2 mol) were reacted with 0.25 mol of *N*-iodosuccinimide or iodine in a mixture of 70% hydrogen fluoride/pyridine and tetramethylene sulfone at room temperature for 30 minutes.

[b] NIS is *N*-iodosuccinimide.

[c] The reaction was carried out in a pressure bomb.

[d] J. Hine, R. G. Ghirardelli, *J. Org. Chem.* **23**, 1550 (1958).

[e] G. A. Olah, J. M. Bollinger, J. Brinich, *J. Amer. Chem. Soc.* **90**, 2587 (1968).

[f] G. A. Olah, J. M. Bollinger, *J. Amer. Chem. Soc.* **90**, 947 (1968).

[g] H. Schmidt, H. Meinert, *Australian J. Chem.* **19**, 161 (1966).

[h] Diiodo compounds were exclusively formed.

[i] The reaction was carried out using equimolar amounts of iodine and silver nitrate.

The reactions with *N*-iodosuccinimide gave usually higher yields of iodofluorinated compounds. By using iodine with pyridine/hydrogen fluoride, iodofluorination occurred readily to disubstituted alkenes, but in the reactions of terminal alkenes and alkynes, diiodo compounds were also obtained. This problem was overcome by adding silver nitrate to quench the iodide ion. In this case the formation of diiodo compound was prohibited. In contrast to hydrofluorination of alkynes giving *gem*-difluorides, iodofluorination of disubstituted alkynes gives vinylic iodofluorine compounds, which are considered as suitable precursors to a wide variety of interesting fluorine compounds. Typical examples of iodofluorination are those of cyclohexene and 1-hexene.

Preparation of 1-Fluoro-2-iodocyclohexane:

Into a mixture of 70% hydrogen fluoride/pyridine (60 ml) and tetramethylene sulfone (30 ml), iodine (7.2 g, 0.03 mol) was dissolved and then to the obtained solution cyclohexene (2.6 g, 0.03 mol) in tetramethylene sulfone (30 ml) was added in 10 min. at room temperature. The reaction mixture was stirred for 20 min. and then was poured into ice-water and extracted with ether. The ether layer was washed with water, aqueous sodium hydrogen carbonate, and water and dried over anhydrous sodium sulfate. After evaporation of ether and unreacted cyclohexene, and usual purification *1-fluoro-2-iodo-cyclohexane* was obtained; yield: 4.9 g (60%); b.p. 73–75°/10 torr.

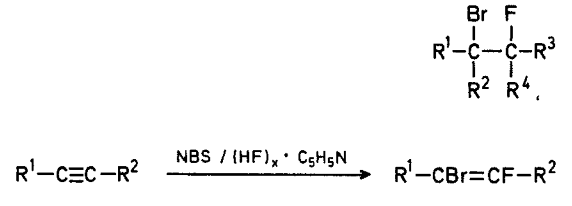
Preparation of 2-fluoro-1-iodohexane:

Into a mixture of 70% hydrogen fluoride/pyridine (60 ml) and tetramethylene sulfone (30 ml), silver nitrate (4.0 g, 0.03 mol) and then iodine (7.2 g, 0.03 mol) were added. Subsequently, 1-hexene (2.5 g, 0,03 mol) dissolved in tetramethylene sulfone (30 ml) was added to the stirred reaction mixture in 10 min. at room temperature. The reaction mixture was worked up in the usual way and *2-fluoro-1-iodohexane* was obtained; yield: 5.3 g (80%); b.p. 72–75°/15 torr. No contamination by 1,2-diiodohexane was observed.

All products were characterized by N.M.R. and infrared spectroscopy which indicated exclusive *trans*-product formation.

Alkenes with low boiling point were reacted in a pressure bomb.

We also succeeded in *bromofluorination* of alkenes and alkynes using *N*-bromosuccinimide or bromine/silver nitrate in hydrogen fluride/tertiary amine reagents. The data are summarized in Table 2.



$$R^1R^2C{=}CR^3R^4 \xrightarrow{\text{NBS or Br}_2\text{–AgNO}_3\text{ / (HF)}_x\cdot \text{C}_5\text{H}_5\text{N}} R^1-\underset{R^2}{\overset{Br}{C}}-\underset{R^4}{\overset{F}{C}}-R^3$$

$$R^1-C\equiv C-R^2 \xrightarrow{\text{NBS / (HF)}_x\cdot \text{C}_5\text{H}_5\text{N}} R^1-CBr{=}CF-R^2$$

Table 2. Bromofluorination of Alkenes and Alkynes[a]

Alkenes or Alkynes	Products	b.p.	Yield (%)
Ethene[b]	1-Bromo-2-fluoroethane[d]	71.5°	30
Propene[b]	1-Bromo-2-fluoropropane[d]	88.5°	40
2-Methylpropene[b]	1-Bromo-2-fluoro-2-methylpropane[e]	95–96°	85
1-Hexene	1-Bromo-2-fluorohexane[d]	60–62°/18 torr	90 80[c]
3-Hexene	3-Bromo-4-fluorohexane	53–55°/15 torr	85
Cyclohexene	1-Bromo-2-fluorocyclohexane[f]	76–78°/16	90 75
Norbornene	7-*anti*-Bromo-2-*exo*-fluoronorbornane[g]	separated by	43
	7-*syn*-Bromo-2-*exo*-fluoronorbornane[g]	gaschromatography	43
2-Butyne	2-Bromo-3-fluorobutene-2	43–45°/300 torr	50
3-Hexyne	3-Bromo-4-fluorohexene-3	55–57°/15 torr	85
Diphenylacetylene	1-Bromo-2-fluoro-1,2-diphenylethene	m.p. 175–178°	95

[a] Alkenes or alkynes (0.2 mol) were reacted with 0.24 mol of *N*-bromosuccinimide in the mixture of 70% hydrogen flurode/pyridine and tetramethylene sulfone at room temperature for 30 min.

[b] The reaction was performed in a pressure bomb.

[c] Bromofluorination was performed using equimolar amounts of bromine and silver nitrate.

[d] F. L. N. Pattison, D. A. V. Peters, *Can. J. Chem.* **43**, 1689 (1965).

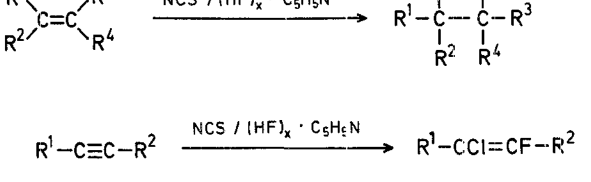
[e] G. A. Olah, J. M. Bollinger, *J. Amer. Chem. Soc.* **90**, 947 (1968).

[f] G. Wittig, U. Mayer, *Chem. Ber.* **96**, 329 (1963).

[g] F. H. Dean, D. R. Marshall, E. W. Warnhoff, F. L. N. Pattison, *Can. J. Chem.* **45**, 2279 (1967).

In contrast to the reaction of iodine, when bromine alone was used, it gave dibromo compounds. By removing bromide ion with silver ion using bromine and silver nitrate, bromofluorination occurred selectively.

Chlorofluorination of alkenes and alkynes can also be carried out conveniently using *N*-chlorosuccinimide in tertiary amine/hydrogen fluoride (Table 3).



$$R^1R^2C{=}CR^3R^4 \xrightarrow{NCS\ /\ (HF)_x \cdot C_5H_5N} R^1{-}\overset{Cl}{\underset{R^2}{C}}{-}\overset{F}{\underset{R^4}{C}}{-}R^3$$

$$R^1{-}C{\equiv}C{-}R^2 \xrightarrow{NCS\ /\ (HF)_x \cdot C_5H_5N} R^1{-}CCl{=}CF{-}R^2$$

Table 3. Chlorofluorination of Alkenes and Alkynes[a]

Alkenes or Alkynes	Products	b.p.	Yield (%)
Propene[b]	1-Chloro-2-fluoropropane	65–67° [c]	35
2-Methylpropene[b]	1-Chloro-2-fluoro-2-methylpropane	71–73° [d]	60
1-Hexene	1-Chloro-2-fluorohexane	58–60°/45 torr	40
3-Hexene	3-Chloro-4-fluorohexane	54–56°/45 torr	80
Cyclohexene	1-Chloro-2-fluorocyclohexane	71–72°/42 torr	85
Norbornene	7-*anti*-Chloro-2-*exo*-fluoronorbornane	separated by	30
	7-*syn*-Chloro-2-*exo*-fluoronorbornane	gaschromatography	45
3-Hexyne	3-Chloro-4-fluorohexene-3	38–40°/20 torr	70
Diphenylacetylene	1-Chloro-2-fluoro-1,2-diphenylethene	m.p. 132–134	95

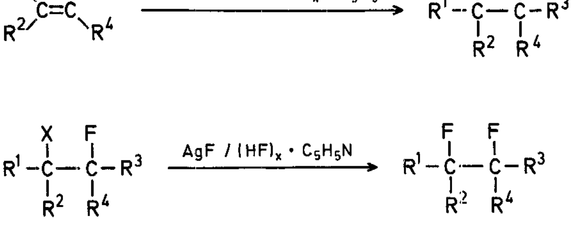
[a] Alkenes or alkynes (0.2 mol) were reacted with 0.24 mol of *N*-chlorosuccinimide in the mixture of 70% hydrogen fluoride/pyridine and tetramethylene sulfone at room temperature for 30 min.

[b] The reaction was performed in the pressure bomb.

[c] I. L. Knunyants, L. S. Gergan, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1966**, 1065.

[d] G. A. Olah, J. M. Bollinger, *J. Amer. Chem. Soc.* **90**, 947 (1968).

Modification of the described halofluorination methods can also be used to carry out *preparation of* vic.*-difluorides* from the corresponding alkenes without isolation of the intermediately formed halofluorinated products. This is conveniently achieved by carring out bromo- and iodofluorination of the alkene with *N*-halosuccinimide/tert. amine/hydrogen fluoride, and then, without isolation of intermediate product, silver fluoride was added to the solution to exchange the bromo-(iodo)-fluoroalkanes to the corresponding difluorides (Table 4).



$$R^1R^2C{=}CR^3R^4 \xrightarrow{NIS\ or\ NBS\ /\ (HF)_x \cdot C_5H_5N} R^1{-}\overset{X}{\underset{R^2}{C}}{-}\overset{F}{\underset{R^4}{C}}{-}R^3$$

$$R^1{-}\overset{X}{\underset{R^2}{C}}{-}\overset{F}{\underset{R^4}{C}}{-}R^3 \xrightarrow{AgF\ /\ (HF)_x \cdot C_5H_5N} R^1{-}\overset{F}{\underset{R^2}{C}}{-}\overset{F}{\underset{R^4}{C}}{-}R^3$$

The procedure is particularly well applicable to disubstituted alkenes, where the desired difluoroalkanes were obtained in excellent yield. Typical is the preparation of 2,3-difluoro-2,3-dimethylbutane.

Table 4. *In Situ* Fluorination of Alkenes

Alkenes	Products	b.p.	Yield (%)
2,3-Dimethylbutene-2[a]	2,3-Difluoro-2,3-dimethylbutane	decomp.[c]	60
3-Hexene[b]	3,4-Difluorohexane	40–42°/100 torr	75
Cyclohexene[b]	1,2-Difluorocyclohexane	48–50°/100 torr	85
Stilbene[a]	1,2-Difluoro-1,2-diphenylethane	70° (decomp.)	95

[a] *N*-Bromosuccinimide was used for the first step of the reaction.

[b] *N*-Iodosuccinimide was used for the first step of the reaction.

[c] Isolated by preparative G.L.C.: G. A. Olah, J. M. Bollinger, *J. Amer. Chem. Soc.* **89**, 4744 (1967).

Preparation of 2,3-Difluoro-2,3-dimethylbutane:

Into a polyethylene flask containing 70% hydrogen fluoride/pyridine solution (100 ml) and ether (100 ml) *N*-bromosuccinimide (18 g, 0.1 mol) was added. To this mixture, cooled by an ice bath, 2,3-dimethylbutene-2 (8.5 g, 0.1 mol) was introduced at 0°, and the reaction mixture was stirred at room temperature for 30 min. Thereafter silver fluoride (19.0 g, 0.1 mol) was added and the reaction continued for 2 hr at room temperature. The reaction mixture was poured into ice-water and extracted with ether. The ether layer was washed with water, aqueous potasssium hydroxide, and water and then dried over anhydrous sodium sulfate. After evaporation of ether at atmospheric pressure carefully using a 10 inch column, *2,3-dimethyl-2,3-difluorobutane* was obtained. As it is not stable to distillation, it should be purified by preparative G.L.C.

^{1}H-N.M.R. (neat, external TMS reference): $\delta = 1.55$ ppm, $J_{HF} = 22$ Hz.
^{19}F-N.M.R. (external CCl_3F reference): ϕ 150.

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[1] Part II. G. A. Olah, M. Nojima, S. Kerekes, *Synthesis*, **1973**, 779.

[2] A. Bowers, *J. Amer. Chem. Soc.* **81**, 4107 (1959).
A. Bowers, L. C. Ibanez, E. Denot, R. Becerra, *J. Amer. Chem. Soc.* **82**, 4001 (1960).
A. Bowers, E. Denot, R. Becerra, *J. Amer. Chem. Soc.* **82**, 4007 (1960).
H. Schmidt, H. Meinert, *Angew. Chem.* **72**, 493 (1960).
E. D. Bergman, I. Shalak, *J. Chem. Soc.* **1959**, 1418.
R. H. Andreatta, A. V. Robertson, *Austr. J. Chem.* **19**, 161 (1966).
G. A. Olah, J. M. Bollinger, *J. Amer. Chem. Soc.* **90**, 947 (1968).
P. W. Kent, K. R. Wood, *J. Chem. Soc.* **1966**, 812.
K. R. Wood, P. W. Kent, D. Fisher, *J. Chem. Soc.* **1966**, 910.
For a summary giving further references see: W. A. Sheppard, C. M. Sharts, *Organic Fluorine Chemistry*, Benjamin, Inc. New York, 1969.