CHEMISTRY LETTERS, pp. 1675-1678, 1987.

Halogen-Exchange Fluorination of Primary Alkyl Halides Using 1B Metal Fluorides-Pyridine Derivatives

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Deep purplish red semicrystaline precipitates were obtained by the treatment of Cu_2O with HF. After calcination at 100 °C or higher temperature, this compound was successfully used as a highly effective halogen-exchange fluorination reagent for primary alkyl halides in the presence of pyridine derivatives. AgF and a mixture of CuF_2 with copper powder also exhibited high activity in the reaction.

Halogen-exchange fluorination of aliphatic halides is the important synthetic way to obtain fluoro compounds.1) Although there are a number of halogen-exchange fluorination methods for primary alkyl halides (RX), they all require extremely prolonged reaction to produce the corresponding fluorides in fairly good yields as shown in Table 2. In our previous report,2) a solution of Cu_2O in anhydrous hydrogen fluoride (HF) with organic bases such as ethers was found to be highly reactive and selective halogen-exchange fluorination reagents for cyclo or tertiary alkyl halides. Application of this solution to RX was found to give lower yields than 20% for the corresponding primary alkyl fluorides (RF) together with considerable amounts of isomeric secondary alkyl fluorides. However, the formation of RF suggests that the halogen exchange of RX with fluoride ion in the presence of Cu_2O in HF - organic bases proceeds not only via Sn1 reaction mode but also partialy through Sn2 mode. We now wish to report here a novel, highly reactive halogen-exchange fluorination method using 1B monovalent metal fluoride - pyridine derivative solutions for RX.

To 20 g of Cu_2O placed in a 100 ml FEP reaction vessel, HF (20 ml) was added in portions under magnetic stirring at -78 °C. Considerable evolution of heat was observed in the initial stage of addition of HF to Cu_2O. After the complete addition of HF, the solution, in which most of Cu_2O remained undissolved, was warmed carefully to 0 °C under an argon atmosphere. In time, the exothermic reaction took place with the evolution of HF gas. The undissolved substance changed from reddish brown to deep purplish red. The resulting solution was allowed to stand for 30 min at 0 °C, another 30 min at room temperature, and then was heated to 50 °C or higher to remove HF. A stable semicrystaline substance thus obtained was slightly hygroscopic, and was crushed before use for the halogen-exchange fluorination. This substance was found to have a highly effective halogen-exchange fluorination activity for primary haloalkanes and is considered to be a CuF-like compound,11) since commercialy available CuF_2 is light

Table 1. The Halogen-Exchange Fluorination of 1-Bromooctane Using a CuF-Like Compound[a,b] and Pyridines

Pyridine derivative	Solvent	Conversion	Product Yield/%[c]	
		%	RF[d]	Octenes
2,2'-Bipyridine[e]	-	99	84	7
2,4,6-Trimethylpyridine	-	56	48	1
2,4,6-Trimethylpyridine[f]	-	97	83	2
2,4,6-Trimethylpyridine	Benzonitrile	57	37	1
2,4,6-Trimethylpyridine	Benzophenone	21	10	0
2,4,6-Trimethylpyridine	Acetophenone	57	33	1
2,4,6-Trimethylpyridine	Decane	13	7	0
2,6-Dimethylpyridine	-	44	34	1
2,4-Dimethylpyridine	-	99	48	2
2-Methyl-5-ethylpyridine	-	99	48	2
Pyridine	-	99	5	0
2-Methyl-pyridine	-	99	41	0
2-Ethyl-pyridine	-	99	65	1
Quinoline	-	99	22	1
2-Metylquinoline	-	30	8	0

a) Prepared by the treatment of Cu_2O with HF. Calcined at 130 °C.
b) Reaction Conditions; Time 45 min, Temp 130 °C, 1-Bromooctane 5 mmol, Solvent 3-10 ml, CuF like compound 13 mmol, CuF/Pyridine derivative=1/2 molar ratio.
c) Based on the substrate. d) 1-Fluorooctane. e) CuF/Bipyridine=1/1 molar ratio.
f) CuF-like compound calcined at 100 °C.

blue powder and is not active as a fluorination agent.

The general reaction procedure of the halogen-exchange fluorination of alkyl halides with 1B-metal fluorides was carried out as follows. 1B-Metal fluoride (1-5 mmol) was placed in a 25-50 ml egg-plant shape flask equipped with a reflux condenser. Then the prescribed amount of a pyridine derivative and an alkyl halide were added respectively. A stream of argon gas is passed through the apparatus to displace the air. The reaction vessel was heated up by using an oil bath under sufficient stirring at the temerature and time indicated in the Tables. The reaction mixture was then cooled to room temperature and organic substances were extracted with ether and identified by ordinary spectroscopic methods. Some of the experimental results are shown in Tables 1 and 2.

As shown in Table 1, the halogen-exchange fluorination of 1-bromooctane was greatly affected by the presence of pyridine derivatives, although pyridine itself was not effective because it reacts with haloalkane to give N-alkylpyridinium salt mainely. The role of pyridine derivatives in the present reaction is considered to serve as ligands coordinated to the CuF-like compound, which generate reactive fluoride ions, as already demonstrated by Sonoda and Kobayashi.[8] The CuF-like compound calcined at 100 °C exhibited the higher halogen-exchange fluorination activity than that at 130 °C. However, the reaction using solvents such as benzonitrile under the same conditions proceeded in a sluggish manner.

Table 2. The Halogen-Exchange Fluorination of Holoalkanes

Reagent	Substrate	Reaction		Product Yield/%[a]	
		Time/h	Temp/°C	RF[b]	By-products
Anion-exchange resins[c,l]	1-Bromooctane	20	86	82	Alkenes(12)
	2-Bromooctane	25	86	20	Alkenes(73)
Aq-KF with phase-transfer catalyst[d]	1-Bromooctane	3.5	160	64	Alkenes(15) Alcohols(8)
	2-Bromooctane	5	160	-	Alkenes(64) Alcohols(8)
18-Crown-6-Complex-KF[e,m]	1-Bromooctane	230	83	92	1-Octene(8)
	2-Bromooctane	150	83	32	Octenes(68)
KF[f,k]	1-Bromooctane	23	135	48	Ethers and Alkenens
Spray-dry KF[g,m]	1-Bromooctane	10	82	65[p]	
CuF_2[h,m,q]	1-Bromooctane	128	82	88	Octenes(2)
$KF-CaF_2$[n,i]	1-Bromododecane	5	160	84	Dodec-1-ene(16)
$KF-CaF_2$[o,j]	1-Bromooctane	48	100	40	Oct-1-ene(2)
CuF[r,t]	1-Bromooctane	0.75	130	83	Octenes(2)
	1-Chlorooctane	3	160	64	Octenes(1)
	1-Tosyloctane	0.75	130	77	None of others
	2-Bromooctane	0.75	130	51	Octenes(32)
	1,10-dibromocctane	3	130	66	
	1,10-dibromocctane	1	130	45	1-Bromo-10-fluorodecane(22)
CuF_2[t]	1-Bromooctane	0.75	130	Trace	
$Cu(0)+CuF_2$[s]	1-Bromooctane	0.75	130	19	Octenes(0.2)
$Cu(0)+CuF_2$[t]	1-Bromooctane	0.75	130	75	Octenes(8)
AgF[t]	1-Bromooctane	0.75	130	99	Octenes(1)
	1-Chlorooctane	0.75	130	86	Octenes(1)
	1-Tosyloctane	0.75	130	97	None of others
	2-Bromooctane	0.5	130	55	Octenes(29)
	1,10-dibromocctane	1	130	90	None of others

a) Based on the substrate. b) The corresponding fluoroalkane to the substrate.
c) Ref. 3. d) Ref. 4. e) Ref. 5. f) Ref. 6. g) Ref. 7. h) Ref. 8.
i) Ref. 9. j) Ref. 10. k) Solvent; Diethylene glycohol. l) Solvent; Hexane.
m) Solvent; Acetonitrile. n) Solvent; Sulpholane. o) Solvent; Tetraglyme.
p) No description about the by-product. q) With 2,2'-Bipyridine.
r) Prepared from Cu_2O and HF, and calcined at 100 °C.
s) Substrate/Reagent=1/5; Reagent/γ-Collidine=1/2 molar ratio respectively.
t) Substrate/Reagent=1/2; Reagent/2,2'-Bipyridine=1/1 molar ratio respectively.

The halogen-exchange fluorination of 1-haloalkanes using CuF-like compound calcined at 100 °C was carried out. Typical experimental results are listed in Table 2 together with the results using commercialy available CuF_2 and AgF, and those reported in literatures. The corresponding fluoroalkanes to substrates were obtained in good yields by the reaction with a CuF-like compound in the presence of γ-collidine at 130 °C for only 0.75-3 h. 1-Tosyloctane also gave a good result to produce 1-fluorooctane under the same conditions. Although a considerable amount of alkenes was formed, secondary-haloalkanes such as 2-bromooctane gave the coressponding fluoroalkanes in better yields than those appering in literatures. Almost a quantitative yield of 1-fluorooctane was obtained in the reaction of 1-halo or tosyloctanes with commercialy available AgF under the same conditions. Commercialy available CuF_2, on the other hand, was not effective for the reaction under the same conditions. However, the activity of halogen-exchange fluorination with CuF_2 was increased in the presence of copper powder and greatly enhanced by the use of bipyridine insted of γ-collidine.

The application of the CuF-like compound and CuF_2-Cu(0) reagent to the fluorination of other substrates having other fuctional groups are under progress.

References

1) R. E. Banks, "Organofluorine Chemicals and Their Industrial Applications," Ellis Horwood LTD, England (1979); N. Ishikawa, " Halogen Chemicals No Saisentan, CMC, Tokyo (1984); M. R. C. Gerstenberger and A. Haas, Angew. Chem., Int. Ed. Engl., 20, 647 (1981).
2) N. Yoneda, T. Fukuhara, S. Nagata, and A. Suzuki, Chem. Lett., 1985, 1693.
3) G. Cainelli and F. Manescalchi, Synthesis, 1976, 472.
4) D. Landini, F. Montanari, and F. Rolla, Synthesis, 1974, 428.
5) C. L. Liottand and H. P. Harris, J. Am. Chem. Soc., 96, 2250 (1974).
6) F. L. M. Pattison and J. J. Norman, J. Am. Chem. Soc., 79, 2311 (1957).
7) N. Ishikawa, T. Kitazume, T. Yamazaki, Y. Mochida, and T. Tatsuno, Chem. Lett., 1981, 761.
8) H. Sonoda, T. Sonoda, and H. Kobayashi, Chem. Lett., 1985, 233.
9) J. H. Clark, A. J. Hyde, and D. K. Smith, J. Chem. Soc., Chem. Commun., 1986, 791.
10) J. Ichihara, T. Matsuo, T. Hanafusa, and T. Ando, J. Chem. Soc., Chem. Commun., 1986, 793.
11) This substance has not been well characterized yet but seems to contain monovalent copper,12) or a mixture of zero and divalent coppers. It has the composition of $CuF \cdot 1/2H_2O$ by the results of differential thermal analylsis, X-ray analysis, atomic absorption spectroscopic analysis, colorimetric determination, oxidation-reduction titration using potassium dichromate, and fluoride ion analysis by the JIS methods.14) X-Ray photoelectron spectroscopy, however, indicated substance on the surface was divalent copper. This may arise from the oxidation of monovalent copper on the surface in the air. In this report, we refer to this substance as a CuF-like compound that is one of 1B metal fluorides.
12) Although some physical and chemical data of CuF appear in the literature,13) the existence of this substance is a long-standing question so far.
13) "Encyclopedia of Chemical Technology," 3rd ed, ed by D. T. Meshri, Ozark-Mahoning Co., The Interscience Encyclopedia Inc., New York (1980), Vol. 10, pp. 719-720 Japanese Reprint Ed., Maruzen Co. Ltd., Tokyo.
14) "Japanese Industrial Standard," Investigated by Japanese Industrial Standards Commitee, Pubrished by Japanese Standards Association (1981), K 0102-1981, p. 94.

(Received June 12, 1987)