Tetrahedron Letters, Vol.31, No.22, pp 3167-3170, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

The Combination of Ammonium Hydrogen Fluoride and Aluminium Fluoride An Efficient Solid Fluoride Source for Halofluorination of Alkenes

Junko Ichihara,* Kotaro Funabiki, and Terukiyo Hanafusa
The Institute of Scientific and Industrial Research,
Osaka University, Mihogaoka, Ibaraki, Osaka 567, Japan

Summary: The combination of ammonium hydrogen fluoride and porous aluminium fluoride (NH_4HF_2-AlF_3) is a useful solid reagent for introducing fluorine to simple alkenes with N-halosuccinimide under sonication to afford the halofluorinated compounds.

Halogen fluoride addition to alkenes is one of the important reactions for preparation of monofluoroaliphatic compounds.[1] Although anhydrous hydrogen fluoride has been conventionally used as a fluoride source, in line with the rapid development of organofluorochemistry various efforts have been made to search for alternatives for the last decade.[2] Recently we have found that the combination of hydrogen fluoride salt and porous aluminium fluoride (MHF_2-AlF_3) is an efficient 'HF' source for epoxide-opening reaction under sonication to give fluorohydrin.[3] In this paper, we report that the combined use of the NH_4HF_2-AlF_3 reagent, N-halosuccinimide and ultrasound provides a useful method for promoting the halofluorination of simple alkenes under solid-liquid two-phase conditions.

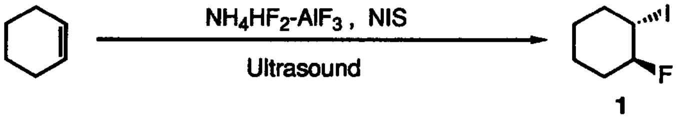
Hydrogen fluoride salts (HF_2 salts) which are easy to handle but less reactive have been so far scarcely used for the halofluorination.[4] For preliminary experiments, the reactivities of these salts were compared in the iodofluorination of cyclohexene with N-iodosuccinimide (NIS) as an electrophile in dimethoxyethane under different conditions (Table 1). HF_2 salts alone promoted somewhat the heterogeneous reaction at 60 °C, but prolonged reaction time or ultrasonic irradiation did not increase the yield of the desired product further (runs 1, 2, 5 and 7). In contrast, the addition of porous aluminium fluoride[5] was effective both to accelerate the reaction and to raise the yield of the desired product (run 3). Sonication was also helpful in the iodofluorination (run 4). In these reactions, the NH_4HF_2-AlF_3 reagent was found to be superior to the KHF_2-AlF_3 or the $NaHF_2$-AlF_3 reagent (runs 4, 6, and 8). The typical experimental conditions are as follows: The heterogeneous mixture of 2 mmol of cyclohexene and 3 mmol of NIS dissolved in dimethoxyethane with the NH_4HF_2-AlF_3 reagent (1:3 molar ratio) containing 8 mmol of NH_4HF_2 was

Table 1. The Heterogeneous Iodofluorination of Cyclohexene Using HF_2 Salt and N-Iodosuccinimide[a]

Run	Fluoride source	Ultrasound[b]	GLC Yield of 1 / % (Time / h)
1	NH_4HF_2	–	15 (1) 19 (6)
2	NH_4HF_2	+	16 (1) 20 (6)
3	NH_4HF_2-AlF_3[c]	–	57 (1) 57 (6)
4	NH_4HF_2-AlF_3[c]	+	75 (1)
5	KHF_2	+	3 (1) 8 (6) 12 (20)
6	KHF_2-AlF_3[c]	+	36 (1) 82 (6)
7	$NaHF_2$	+	2 (1) 13 (6) 46 (20)
8	$NaHF_2$-AlF_3[c]	+	25 (1) 78 (6)

[a] The reaction of cyclohexene (2 mmol) with fluoride source (8 mmol) and NIS (3 mmol) was carried out in dimethoxyethane (10 cm^3) at 60 °C. [b] + : A thermostated ultrasonic cleaner (Bransonic, 100 W, 45 kHz) was used. – : Magnetic stirrer was used. [c] Molar ratio of MHF_2 to AlF_3 is 1:3.

subjected to ultrasonic irradiation at 60 °C for 1 h to afford the desired product in 75% glc yield. Simple work-up by filtration, washing by aq. sodium thiosulfate, evaporation of the solvent, and purification of the residue with preparative thin layer chromatography gave trans-1-fluoro-2-iodocyclohexane (1) in 52% yield.



1

Successful sonochemical iodofluorination of some simple alkenes with the same reagents are summarized in Table 2. Table 3 shows the results of bromofluorination with N-bromosuccinimide (NBS) as an electrophile under analogous conditions. The reactivities of these reagents were dependent on a solvent used. Dimethoxyethane or 1,2-dichloroethane was favorable as a solvent for the iodofluorination, and diethyl ether or diisopropyl ether for the bromofluorination. Some of the bromofluorinations smoothly proceeded without ultrasonic irradiation. The lower yields of the bromofluorinated products than those of the iodofluorinated ones are due to the formation of such side products as the corresponding dibromides in about 20% yield.[6] However, by column chromatography the desired product could be easily separated from byproducts. The regioselectivity in the addition of a fluorine to the double bond in a substrate was not so high in some reactions, but the stereoselectivity in the addition of two different halogens was anti-specific in the reaction of cyclohexene.

Although the mechanism of the solid-liquid two-phase reaction studied here was not elucidated in detail, we consider at least that the activation mechanism of HF_2 salts by both porous aluminium fluoride and ultrasound may be similar to the epoxide-opening reaction reported previously.[3] Thus, the halofluorination is also stoichiometrically represented by equation (1).

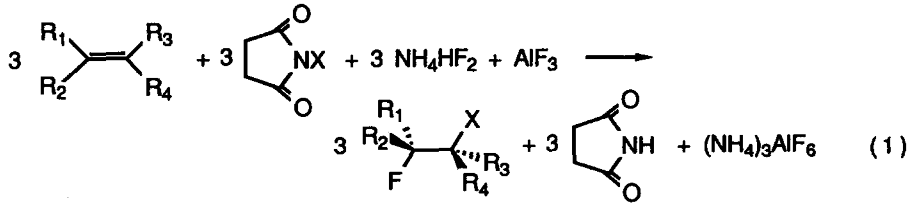
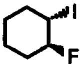
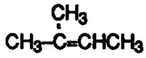
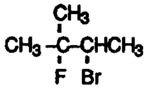
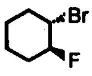
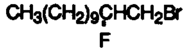
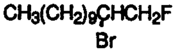
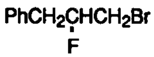
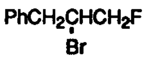

(1)

Table 2. Sonochemical Iodofluorination of Alkenes Using the NH_4HF_2-AlF_3 Reagent and NIS[a]

Alkene	Solvent	Temp / °C	Time / h	Product	Yield / %[b]	
$CH_3\text{-}\overset{CH_3}{C}{=}CHCH_3$	DME	30	2	$CH_3\text{-}\overset{CH_3}{\underset{F}{C}}\text{-}\underset{I}{C}HCH_3$	(85)	56
	DME	60	1		(75)	52
	$ClCH_2CH_2Cl$	60	3		(70)	48
$CH_3(CH_2)_9CH{=}CH_2$	$ClCH_2CH_2Cl$	60	6	$CH_3(CH_2)_9\underset{F}{C}HCH_2I$ $CH_3(CH_2)_9\underset{I}{C}HCH_2F$	77 ·· 23 [c]	64
$PhCH_2CH{=}CH_2$	$ClCH_2CH_2Cl$	60	6	$PhCH_2\underset{F}{C}HCH_2I$ $PhCH_2\underset{I}{C}HCH_2F$	74 ·· 26 [c]	77
$PhCH{=}CH_2$	DME	25	4	$Ph\underset{F}{C}HCH_2I$	—	54
$Ph\text{-}\overset{CH_3}{C}{=}CH_2$	$ClCH_2CH_2Cl$	60	5	$Ph\text{-}\overset{CH_3}{\underset{F}{C}}\text{-}CH_2I$	—	54
(E)-$CH_3CH{=}CHCH_2OH$	DME	50	2	$CH_3\underset{F}{C}H\underset{I}{C}HCH_2OH$ $CH_3\underset{I}{C}H\underset{F}{C}HCH_2OH$	77 ·· 23 [c]	60

[a] The mixture of an alkene (2 mmol) with the NH_4HF_2-AlF_3 reagent (1 : 3 molar ratio, 8 mmol) and NIS (3 mmol) in solvent (10 cm^3) was subjected to ultrasonic treatment. [b] Isolated yield. Figures in parentheses show glc yields. [c] Relative ratio determined by ^{19}F NMR.

Table 3. Bromofluorination of Alkenes Using the NH_4HF_2-AlF_3 Reagent and NBS[a]

Alkene	Solvent	Temp / °C	Time / h	Product	Yield / %[b]	
 $CH_3C(CH_3){=}CHCH_3$	Et_2O	20[f]	2	 $CH_3C(CH_3)(F)CH(Br)CH_3$	68[c]	
	Et_2O	30	1		50[d]	27
		20[f]	2		54[d]	36
$CH_3(CH_2)_9CH{=}CH_2$	i-Pr_2O	30	5	 $CH_3(CH_2)_9CH(F)CH_2Br$  $CH_3(CH_2)_9CH(Br)CH_2F$	75 25 [e]	47
$PhCH_2CH{=}CH_2$	i-Pr_2O	40	2	 $PhCH_2CH(F)CH_2Br$  $PhCH_2CH(Br)CH_2F$	74 26 [e]	52

[a] See in text. [b] Unless otherwise mentioned isolated yield are shown. [c] Yield determined by ^{19}F NMR. [d] Glc Yield. [e] Relative ratio determined by ^{19}F NMR. [f] Mechanical stirring without ultrasound.

Powder X-ray diffraction analysis of the inorganic solid materials recovered after the reaction showed clearly the formation of ammonium hexafluoroaluminate ($(NH_4)_3AlF_6$). The results confirm the above equation.

Acknowledgement. We are indebted to the Material Analysis Center of ISIR for ^{19}F NMR measurements.

References and Notes

1. J. T. Welch, Tetrahedron, **43**, 3123 (1987); J. Mann. Chem. Soc. Rev., **16**, 381 (1987); C. M. Sharts and W. A. Sheppard, Org. React., **21**, 137 (1972).
2. G. A. Olah, J. T. Welch, Y. D. Vankar, M. Nojima, I. Kerekes, and J. A. Olah, J. Org. Chem., **44**, 3872 (1979); G. A. Olah, M. Nojima, and I. Kerekes, Synthesis, **1973**, 780; A. Gregorcic and M. Zupan, J. Fluorine Chem. **24**, 291 (1984); G. Alvernhe and A. Laurent, and G. Haufe, Synthesis, **1987**, 562; S. Rozen and M. Brand, J. Org. Chem., **50**, 3342 (1985); G. E. Hearley, J. M. Janes, S. R. Stark, and B. L. Robinson, Tetrahedron Lett., **26**, 1811 (1985); R. D. Evans and J. H. Schauble, Synthesis, **1987**, 551; T. Ando, D. G. Cork, M. Fujita, T. Kimura, and T. Tatsuno, Chem. Lett., **1988**, 1877; M. Shimizu, Y. Nakahara, and H. Yoshioka, J. Chem. Soc., Chem. Commun., **1989**, 1881.
3. J. Ichihara and T. Hanafusa, J. Chem. Soc., Chem. Commun., **1989**, 1848.
4. F. Campus, E. Chamorro, V. Gasol, and A. Guerrero, J. Org. Chem., **54**, 4294 (1989).
5. The preparation of porous aluminium fluoride is described in ref. 3.
6. In the case of cyclohexene, the use of NH_4HF_2 in the absence of aluminium fluoride gave the corresponding dibromides as a major product under the similar conditions. Thus, aluminium fluoride rather suppresses the side reaction by activation of hydrogen fluoride salt.

(Received in Japan 13 February 1990)