vic-Difluorination of Fluoroalkenes with Xenon Difluoride: The Effect of Fluorine Substituents on the Reaction of Alkenes with Xenon Difluoride

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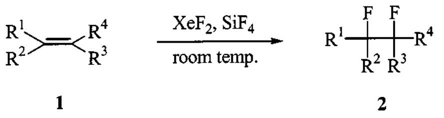
vic-Difluorination proceeds by the reaction of fluoroalkenes with xenon difluoride to afford the corresponding fluorinated compounds. From the reaction with polyfluoroalkenes, the products are obtained in high to excellent yields. In this reaction, the fluorine atom substituent of alkene stabilizes the cation intermediate and suppresses side-reactions such as rearrangement.

vic-Difluorination of alkenes is one of the most fundamental methods of introducing fluorine atoms into organic molecules,[1] and has been widely applied to the synthesis of organofluorine compounds such as fluorine-containing biologically active compounds.[2] Several kinds of fluorinating agents, other than elementary fluorine,[3] for the *vic*-difluorination of alkenes have been studied and xenon difluoride (XeF_2) has proved to be very successful.[4−6] However, *vic*-difluorination with XeF_2 has only been successfully applied to phenyl-substituted alkenes. If aliphatic alkenes are reacted with xenon fluoride, the reaction is generally accompanied by rearrangement and the product of *vic*-difluorination is not predominant.[7][8]

Recently, we have investigated the application of silicon tetrafluoride (SiF_4) in the fluorination reaction;[9−11] we found that *vic*-difluorination of phenylalkenes with XeF_2 is enhanced by SiF_4.[12] In the course of this research, we have investigated the reaction of aliphatic alkenes with XeF_2 (Scheme 1). In this study we found that, in the case of the reaction with fluoroalkenes, the fluorine atom substituent suppresses side-reactions such as rearrangement, so that the major reaction products are those of *vic*-difluorination. We have also found that, in the case of polyfluoroalkenes, the corresponding products are obtained in high to excellent yields from this reaction.

Initially, the reactions of several substituted ethylenes (**1a−d**) with XeF_2 in the presence of SiF_4 were attempted (Table 1, entry 1−6). The unsubstituted ethylene **1a** gave the corresponding *vic*-difluoride **2a**, but significant amounts of the *gem*-difluoride and trifluoride were also obtained (entry 1). The vinyl ether **1b** did not afford the *vic*-fluoride but only polymeric material (entry 2). In the case of the fluoroethylene **1c**, however, *vic*-difluorination proceeded and the corresponding product **2c** was obtained in high yield. The yield did not depend on the catalyst used (entry 3−5). Ethylene substituted with a halogen atom other than fluorine **(1d)** gave predominantly the *gem*-difluoride (entry 6). This result shows that fluorine plays an important role as a substituent in suppressing side reactions. This effect of the fluorine substituent was also examined in the case of the other fluoroalkenes. *vic*-Difluorination of fluoroalkenes substituted with alkyl groups (**1f,h**) proceeded with better yields than the reaction of the corresponding unsubstituted alkenes (**1e,g**), although the yields were still modest (entry 7−10).



	R^1	R^2	R^3	R^4
a	H	H	H	H
b	EtO	H	H	H
c	F	H	H	H
d	Br	H	H	H
e	CH_3	H	CH_3	H
f	F	CH_3	CH_3	H
g	H	$-(CH_2)_4-$		H
h	F	$-(CH_2)_4-$		H
i	F	F	H	H
j	F	F	F	H
k	F	F	F	Cl
l	CF_3	F	F	F

Scheme 1. Reaction of aliphatic alkene **1** with XeF_2 in the presence of SiF_4

vic-Difluorination of polyfluoroalkenes (**1i−l**) was also examined and the results are summarized in Table 2. The reactions of polyfluoroethylenes were successful and the corresponding products were obtained in high to excellent yields (entry 1−3). Although the reaction of perfluoropropene (**1l**) needed a higher reaction temperature, the product **2l** was also obtained in excellent yield (entry 4).

The substituent effect could be explained by the following reaction mechanism. In the reaction of alkenes with XeF_2, it has been suggested that the reaction proceeds via a fluorinated cationic intermediate (**3**, Figure 1).[13] When R is hydrogen or a halogen atom other than fluorine, migration or elimination proceeds (route **b**, **c**, or **e**) because of the low nucleophilicity of the fluoride anion. When R is an alkoxy

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Table 1. Effect of substituent on *vic*-difluorination of substituted alkenes[a]

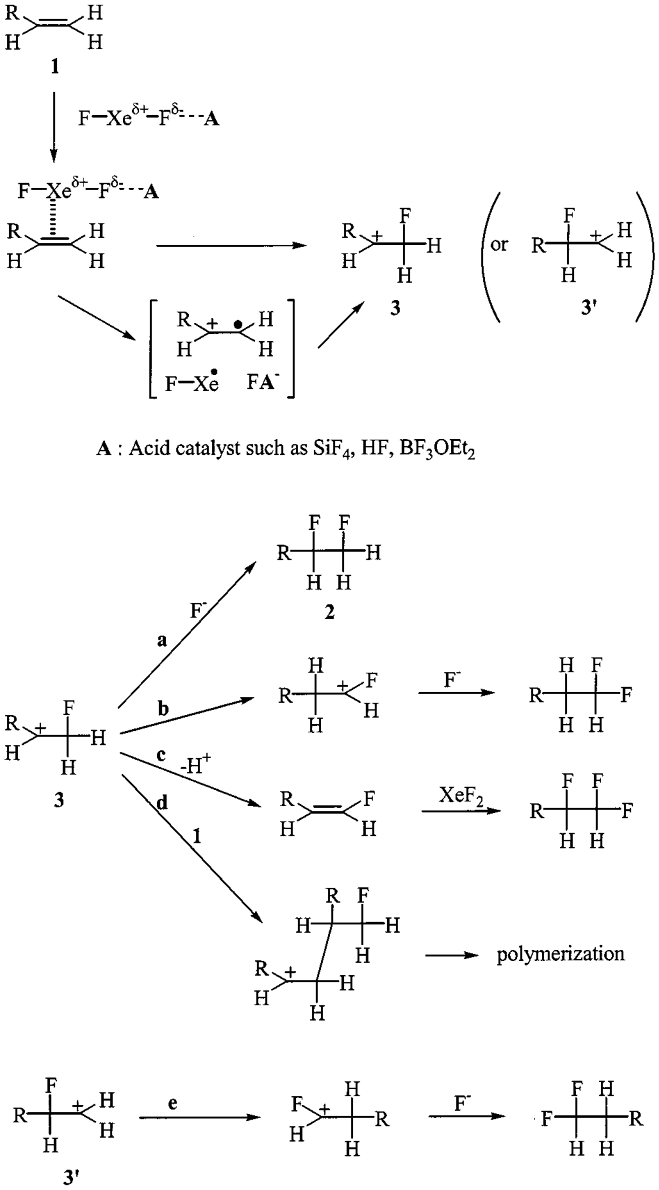
Entry	Substrate	Time (h)	Yield[b] of **2** (%)	Note
1	**1a**	24	63	c
2	**1b**	0.5	0	d
3	**1c**	5	93	–
4	**1c**	5	91	e
5	**1c**	5	91	f
6	**1d**	10	21	g
7	**1e**	16	9	h
8	**1f**	2	33	i
9	**1g**	16	trace	j,k
10	**1h**	2	34	k

[a] Substrate (1 mmol), XeF_2 (1.2 mmol) and SiF_4 (1.2 mmol) were agitated at room temperature. – [b] Entry 1–6: isolated yield. Entry 7–10: yields were determined by ^{19}F NMR analysis of the crude products ($C_6H_5CF_3$ as internal standard). – [c] CHF_2CH_3 (25%) and CHF_2CH_2F (9%) were obtained as by-products. – [d] Polymeric material was obtained. – [e] Hydrogen fluoride (0.8 mmol) was used instead of SiF_4. – [f] Boron trifluoride–diethyl ether (0.1 mmol) was used instead of SiF_4. – [g] Major product was CHF_2CH_2Br (53%). – [h] Major product was $CH_3CF_2CH_2CH_3$ (51%). – [i] $CH_3CF_2CH{=}CH_2$, $CH_3CF_2CH_2CH_2F$, $CH_3CF_2CH_2CH_3$, etc. were obtained as by-products. – [j] Mixture of many products. – [k] Tarry matter was formed.

Table 2. *vic*-Difluorination of polyfluoroalkenes[a]

Entry	Substrate	Time (h)	Yield[b] of **2** (%)
1	**1i**	6	94
2	**1j**	3	99
3	**1k**	4	93
4[c]	**1l**	13	95

[a] Substrate (1 mmol), XeF_2 (1.2 mmol) and SiF_4 (1.2 mmol) were agitated at room temperature. – [b] Isolated yield. – [c] The reaction was carried out at 90°C.



Scheme 2. Mechanism for reaction of alkene with XeF_2

group, nucleophilic attack at the alkene causes polymerization (route **d**) as the nucleophilicity of **1** is increased by the alkoxy group. On the other hand, when R is a fluorine atom, these undesirable reactions are suppressed and *vic*-difluorination predominates (route **a**) as the fluorine atom stabilizes **3** by a mesomeric interaction of its unshared electron pair and decreases the nucleophilicity of **1** by its inductive electron-withdrawing effect.[14] If the molecule contains both a fluorine atom and alkyl groups at the alkene (**1f,h**), however, the side-reactions would not be completely suppressed because the alkyl group enables cation migration to the substituent and increases the nucleophilicity of **1**.[15]

In conclusion, we have shown the effect of the substituent on the reaction of alkenes with XeF_2. In the case of fluoroalkenes, the fluorine atom substituent suppresses side-reactions such as rearrangement and polymerization, and *vic*-difluorination predominates

Experimental Section

General: All of the reagents are commercially available. – IR: Japan Spectroscopic FT-IR 8900. – NMR: JEOL JNM-EX270 (270 MHz). For ^1H NMR, $CDCl_3$ as solvent, TMS as internal standard; for ^{19}F NMR, $CDCl_3$ as solvent, $CFCl_3$ as internal standard.

Fluorination of Alkenes with XeF_2. General Procedure: XeF_2 (1.2 mmol) was placed in a stainless steel reactor equipped with a stop valve. The substrate (1 mmol) and SiF_4 (1.2 mmol) were introduced into the reactor at −196°C from a vacuum line. The reactor was warmed to ambient temperature and shaken. After the reaction was completed, SiF_4 was removed from the reaction mixture by treatment with sodium fluoride and water, and the crude product was purified by trap-to-trap distillation. The products were identified by comparison of their IR, ^1H NMR, and ^{19}F NMR spectra with those of authentic samples.

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[15] It has been reported that *vic*-difluorination of 1-fluoro-4-phenylcyclohexene with XeF_2 in the presence of three equivalents of $AgBF_4$ afforded the corresponding product in 90% yield although the substrate is an alkyl-substituted fluoroalkene.[16] However, this result would appear to be very specific and seems to depend on the substrate − *vic*-difluorination of 1-fluorocyohexene under the same reaction conditions resulted in less than 30% yield according to our experiment.

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