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Monofluorination of fluorinated ethers with high-valency metal fluorides

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Abstract

Fluorinated ethers were fluorinated by high-valency metal fluorides such as MnF_3, CoF_3, and $KCoF_4$. The monofluorinating reactivities of these reagents with 2,2,2-trifluoroethyl difluoromethyl ether, bis(2,2,2-trifluoroethyl) ether, and 2-chloro-1,1,2-trifluoroethyl methyl ether follow the order $MnF_3 > CoF_3 > KCoF_4$. The order of monofluorination reactivity with fluorinated ethers did not agree with that of gem-difluorohydrofluorocarbons ($CoF_3 > MnF_3 > KCoF_4$). Regioselective monofluorination of 2,2,2-trifluoroethoxy compounds with MnF_3 was achieved at the methylene position adjacent to the trifluoromethyl group. © 1997 Elsevier Science S.A.

Keywords: Monofluorination; High-valency metal fluoride; Manganese(III) fluoride; Fluorinated ethers; Chlorofluorinated ether

1. Introduction

Fluorinated ethers have numerous applications such as inhalation anaesthetics [1], lubricating oils [2], solvents, refrigerants, and cleaning reagents [3]. The development of chlorofluorocarbon (CFC) alternatives which are environmentally friendly is most urgent [4]. One possible CFC alternative is fluorinated ether [5]. Because fluorinated ether compounds have no chlorine, their ozone depletion potential is zero; furthermore, their physical and chemical properties are similar to those of CFCs [6].

High-valency metal fluorides (HVMFs) (MnF_3, CoF_3, $KCoF_4$) have been used as important fluorinating reagents, particularly for exhaustive fluorinations of organic compounds by the Fowler process [7]. Tatlow and coworkers have extensively investigated their use for fluorination of alkanes, cycloalkanes, and aromatic compounds [8,9]. In most cases, these reactions were carried out at high temperatures, and monofluorination, which is useful for preparing fluorinated ethers, was not achieved because of small differences between reactivities of C–H bonds in the reactants. In addition, HVMFs are strong Lewis acids, thus some C–O–C bond cleavage occurs in ethers during the fluorination process [10]. It is well known that if some fluorine or chlorine is already present in the organic substrate, the number of undesirable side reactions is markedly reduced [11–13]. In our previous paper, we described the monofluorination of hydrofluorocarbons with 2–5 carbon atoms by CoF_3 [14].

1,2,2,2-Tetrafluoroethyl difluoromethyl ether is a commonly used as an inhalation anaesthetic [15]. This compound was obtained by fluorinating 2,2,2-trifluoroethyl difluoromethyl ether using molecular fluorine. In this fluorination, both conversion rate of the starting compound and selective formation of the desired product are low. We attempted to change one of the C–H bonds to a C–F bond in 2,2,2-trifluoroethyl difluoromethyl ether with HVMFs, and found suitable monofluorination conditions. In this paper we describe the monofluorination reactivity of various HVMFs such as MnF_3, CoF_3 and $KCoF_4$ with fluorinated ethers. The monofluorinating reactivities of these reagents with 2,2,2-trifluoroethyl difluoromethyl ether, bis(2,2,2-trifluoroethyl)ether, and 2-chloro-1,1,2-trifluoroethyl methyl ether follow the order $MnF_3 > CoF_3 > KCoF_4$.

2. Experimental

2.1. General

All volatile compounds were handled in glass and stainless steel vacuum systems similar to those previously described [16]. Amounts of volatile products were determined by PVT measurements. ^{1}H- and ^{19}F-NMR spectra (chemical shifts in ppm from internal reference) were taken at 25 °C on a JEOL EX-270 (270 MHz) spectrometer with $(CH_3)_4Si$

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and $CFCl_3$, respectively, as internal references in $CDCl_3$ (as solvent). Spectral data for all compounds are cited in the literature [11,17,18] except for $CF_3CFHOCH_2CF_3$ and $CF_3CF_2OCH_2CF_3$.

2.2. Reagents

All reagents were obtained from commercial sources. Fluorine was used after passing through a NaF scrubber. Sodium fluoride and high-valency metal fluorides (MnF_3, CoF_3, and $KCoF_4$) were purchased from Hashimoto Kasei Co., Japan. Fluorinated ethers were obtained at PCR guaranteed grade. Solids were dried under vacuum and liquids were distilled under vacuum before use.

2.3. General procedure for the fluorination of fluorinated ethers and chlorofluorinated ether with HVMFs

A typical procedure for the fluorination of fluorinated ethers or chlorofluorinated ether (Eqs. (1)–(3)) is as follows. High-valency metal fluoride (200 mmol) was placed into a batchwise reactor [14]. The reactant (3 mmol) was introduced into the reactor at − 196 °C using a vacuum line system. The reactor was allowed to warm up slowly to ambient temperature (20 °C) for 1 h, then heated at the temperature and for the times indicated in Tables 1–3. It was then cooled to − 196 °C, and the volatile products were pumped out. Hydrogen fluoride was removed from the crude mixture by adding dried sodium fluoride (0.2 g). The products were identified by ^{19}F-NMR and ^{1}H-NMR spectroscopy. The yields of the products and recoveries of reactants were identified by ^{19}F-NMR spectroscopy ($CFCl_3$ was used as an internal reference). The spent metal fluoride was subsequently regenerated at 200–250 °C in the presence of elementary fluorine before the next fluorination.

Table 1
Fluorination of $CF_3CH_2OCF_2H$ with various HVMFs

HVMF	Temp. (°C)	Time (h)	Recovery [a] (%)	Product yield [a] (%)	
				2	**3**
MnF_3	75	6	3	85	5
MnF_3	100	2	25	72	0
CoF_3	100	2	90	10	0
CoF_3	200	1	25	65	3
$KCoF_4$	100	2	100	0	0
$KCoF_4$	200	1	90	10	0

[a] Yields and recovery of $CF_3CH_2OCF_2H$ were determined by ^{19}F-NMR spectroscopy.
2, $CF_3CFHOCF_2H$; **3**, $CF_3CF_2OCF_3$.

Table 2
Fluorination of $CF_3CH_2OCH_2CF_3$ with various HVMFs

HVMF	Temp. (°C)	Time (h)	Recovery [a] (%)	Product yield [a] (%)	
				5	**6**
MnF_3	50	1	80	15	0
MnF_3	100	1	20	63	5
MnF_3	100	2	0	15	22
CoF_3	50	1	100	0	0
CoF_3	100	1	39	52	0
CoF_3	200	1	0	20	21
$KCoF_4$	50	1	100	0	0
$KCoF_4$	100	1	100	0	0
$KCoF_4$	200	1	95	5	0

[a] Yields and recovery of $CF_3CH_2OCH_2CF_3$ were determined by ^{19}F-NMR spectroscopy.
5, $CF_3CFHOCH_2CF_3$; **6**, $CF_3CF_2OCH_2CF_3$.

Table 3
Fluorination of $CHClFCF_2OCH_3$ with various HVMFs

HVMF	Temp. (°C)	Time (h)	Recovery [a] of **7** (%)	Yield [a] of **8** (%)	Selectivity of **8** (%)
MnF_3	0	1	100	0	0
MnF_3	50	1	90	7	70
MnF_3	50	5	30	45	64
MnF_3	100	1	0	8	8
CoF_3	0	1	100	0	0
CoF_3	50	1	100	0	0
CoF_3	100	1	80	10	50
$KCoF_4$	50	1	100	0	0
$KCoF_4$	100	1	100	0	0
$KCoF_4$	200	1	95	3	60

[a] Yield and recovery were determined by ^{19}F-NMR spectroscopy.
8, $CHClFCF_2OCH_2F$.

3. Results and discussion

3.1. Fluorination of 2,2,2-trifluoroethyl difluoromethyl ether with HVMFs

First, we examined the monofluorination reactivity of the various metal fluorides studied. The fluorination of 2,2,2-trifluoroethyl difluoromethyl ether (**1**) with various metal fluorides is summarized in Table 1. The reactions proceed according to Eq. (1).

$$\underset{\mathbf{1}}{CF_3CH_2OCF_2H}$$

(HVMFs; MnF_3, CoF_3, $KCoF_4$)

$$\xrightarrow{\text{HVMFs}} \underset{\mathbf{2}}{CF_3CFHOCF_2H} + \underset{\mathbf{3}}{CH_3CF_2OCF_3} \qquad (1)$$

2,2,2-Trifluoroethyl difluoromethyl ether (**1**) was fluorinated with a series of metal fluorides to give the major product 1,2,2,2-tetrafluoroethyl difluoromethyl ether (**2**). The monofluorination reactivity of each metal fluoride differs, following the order $MnF_3 > CoF_3 > KCoF_4$. When **1** was fluorinated with MnF_3 for 6 h at 75 °C, **2** was the major product at 85% yield with 3% recovery of **1**, and perfluoroethyl methyl ether **3** was obtained as a by-product in low yield. Fluorination of

1 with MnF_3 for 2 h at 100 °C yielded 72% of **2**. Fluorination of **1** with CoF_3 for 2 h at 100 °C gave **2** in 10% yield with 90% recovery of **1**. When fluorination temperature was raised to 200 °C for 1 h, **2** was obtained at 65% yield with 3% of **3**. Fluorination of **1** with $KCoF_4$ for 2 h at 100 °C did not proceed; however, when the reaction temperature was raised to 200 °C, the monofluorinated compound **2** was obtained at 10% yield. From these results, MnF_3 was found to be the most effective monofluorinating reagent of **1**.

3.2. Fluorination of bis (2,2,2-trifluoroethyl) ether with various HVMFs

The fluorination of bis(2,2,2-trifluoroethyl) ether (**4**) with various HVMFs are summarized in Table 2. The reaction proceeds according to Eq. (2).

$$\underset{\mathbf{4}}{CF_3CH_2OCH_2CF_3}$$

$$\xrightarrow{\text{HVMFs}} \underset{\mathbf{5}}{CF_3CFHOCH_2CF_3} + \underset{\mathbf{6}}{CF_3CF_2OCH_2CF_3} \quad (2)$$

Bis(2,2,2-trifluoroethyl) ether (**4**) was fluorinated with MnF_3 at 50 °C for 1 h, and a monofluorinated compound, $CF_3CFHOCH_2CF_3$ (**5**), was obtained as the major product at 15% yield. When the reaction temperature was raised from 50 °C to 100 °C, the yield of **5** increased to 63%. Extending the reaction time at 100 °C led to a decrease in the yield of **5** and an increase in the yield of the by-product $CF_3CF_2OCH_2CF_3$ (**6**). Fluorination of **4** with CoF_3 for 1 h at 100 °C gave mainly **5** at 52% yield. When the reaction temperature was increased to 200 °C, the yield of **5** decreased to 20%, and **6** was formed. Fluorination of **4** with $KCoF_4$ for 1 h at 100 °C did not occur. When the reaction temperature was raised to 200 °C, **5** was obtained at 5% yield. The monofluorination reactivity of each metal fluoride differs, following the order $MnF_3 > CoF_3 > KCoF_4$.

Compound **5**: ^{1}H-NMR (from TMS) δ: 4.30 (q, 2H, $-OCH_2-$, $J_{HF} = 8.0$ Hz); 5.50 (dq, 1H, $-CHFO-$, $J_{HF} = 59.4$ Hz, $J_{HF} = 3.0$ Hz) ppm. ^{19}F-NMR (from $CFCl_3$) δ: 75.3 (td, 3F, $-CF_3$, $J_{HF} = 8.0$ Hz, $J_{FF} = 2.0$ Hz); 84.2 (dd,3F, CF_3-, $J_{FF} = 5.9$ Hz, $J_{HF} = 3.0$ Hz); 145.1 (dqq, 1F, $-CHFO-$, $J_{HF} = 59.0$ Hz, $J_{FF} = 6.0$ Hz, $J_{FF} = 2.0$ Hz) ppm. **6**: ^{1}H-NMR (from TMS) δ:4.31 (q, 2H, $-CH_2O-$, $J_{HF} = 7.5$ Hz) ppm. ^{19}F-NMR (from $CFCl_3$) δ: 75.2 (t, 3F, CF_3-, $J_{HF} = 7.5$ Hz); 86.5 (s, 3F, $-CF_3$); 91.9 (s, 2F, $-OCF_2-$) ppm.

3.3. Fluorination of 2-chloro-1,1,2-trifluoroethyl methyl ether with HVMFs

The results of fluorination of 2-chloro-1,1,2-trifluoroethyl methyl ether (**7**) with various metal fluorides are shown in Table 3. The reactions proceed according to Eq. (3). 2-Chloro-1,1,2-trifluoroethyl fluoromethyl ether (**8**) was obtained as the main product.

$$\underset{\mathbf{7}}{CHClFCF_2OCH_3} \xrightarrow{\text{HVMFs}} \underset{\mathbf{8}}{CHClFCF_2OCH_2F} \quad (3)$$

2-Chloro-1,1,2-trifluoroethyl methyl ether (**7**) was fluorinated with MnF_3 at 50 °C for 1 h, and a monofluorinated compound, 2-chloro-1,1,2-trifluoroethyl fluoromethyl ether (**8**), was obtained at 7% yield as the major product (Table 3). Prolonging the reaction time to 5 h increased the yield of **8** to 45%. When the reaction temperature was raised from 50 °C to 100 °C, the yield of **8** was decreased to 8% and a large amount of polyfluorinated by-products were generated (data not shown).

Fluorination of **7** with CoF_3 for 1 h at 50 °C did not proceed. When the reaction temperature was raised to 100 °C, **8** was obtained at 10% yield. Fluorination of **7** with $KCoF_4$ for 1 h at 100 °C did not proceed; however, when the reaction temperature was raised to 200 °C, as small amount of **8** was obtained. The monofluorination reactivity of each metal fluoride differs, following the order $MnF_3 > CoF_3 > KCoF_4$.

Clayton et al. reported that **7** was fluorinated with CoF_3 in a flow-type reactor and **8** was obtained as the main product, although at a low yield [11]. This monofluorination tendency agreed with that observed in the present work.

The order of fluorinating reactivities of HVMFs for fluorinated ethers differs from those for hydrofluorocarbons. This may be due to differences in the coordination ability between fluorinated ethers and hydrofluorocarbons on metal fluorides. Calculations using the molecular orbital method should be performed to solve this problem [19,20], and are under way.

4. Conclusions

MnF_3 is the most effective compound for the monofluorination of fluorinated ethers. Monofluorination by MnF_3 is advantageous in that it has an apparent stabilizing effect on the ether linkage of fluorinated ethers. MnF_3 was found to be useful for monofluorinating fluorinated ethers, which cannot be achieved with elemental fluorine or by electrochemical fluorination.

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