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Journal of Fluorine Chemistry 127 (2006) 79-84



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Fluorination of fluoro-cyclobutene with high-valency metal fluoride

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Received 22 September 2005; received in revised form 13 October 2005; accepted 14 October 2005 Available online 28 November 2005

Abstract

Fluorinations of 1,4,4-trifluorocyclobutene and 3,3,4,4-tetrafluorocyclobutene using high-valency metal fluorides such as CoF_3 , MnF_3 , AgF_2 , CeF_4 and $KCoF_4$, and elemental fluorine were examined. In these reactions with CoF_3 and MnF_3 , *vic*-difluorination proceeded mainly. While, 1,4,4-trifluorocyclobutene yielded 3,3,4,4-tetrafluorocyclobutene, and 3,3,4,4-tetrafluorocyclobutene yielded 1,3,3,4,4-pentafluorocyclobutene mainly in the case of AgF_2 . The further fluorinated products were increased under severer conditions. Also, the plausible reaction mechanism was suggested.

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Keywords: Fluoro-cyclobutene; High-valency metal fluoride; Fluorination; vic-Difluorination

1. Introduction

vic-Difluorination of alkenes is one of the convenient methods to introduce fluorine atom into organic compounds [1], and utilized for the preparation of organofluorine compounds such as biologically active compounds [2–4]. Alkyl perfluor-oalkyl ethers could be also prepared by *vic*-difluorination of corresponding perfluorovinyl ethers using high-valency metal fluorides [5]. High-valency metal fluorides such as cobalt trifluoride (CoF₃), manganese trifluoride (MnF₃), silver difluoride (AgF₂), cerium tetrafluoride (CeF₄) and potassium tetrafluorocobaltate (KCoF₄) have been reported to be a mild *vic*-difluorinating agent of various alkenes compared with elemental fluorine [6–8].

Fluoro-cyclobutanes could be conveniently prepared by [2 + 2] cyclization reaction of fluorinated olefins such as tetrafluoroethylene (TFE) [9], chlorotrifluoroethylene (CTFE) [10] and 1,1-dichloro-2,2-difluoroethylene [11]. Furthermore, various fluoro-cyclobutanes could be prepared by the cross-coupling cyclization reaction of two kinds of alkenes [10,12]. For example, the reaction of TFE and ethylene afforded 1,1,2,2-

tetrafluorocyclobutane [12]. Also, fluoro-cyclobutenes could be prepared easily from the corresponding cyclobutanes by dehalogenation or dehydrohalogenation.

In this paper, the fluorinations of fluoro-cyclobutenes such as 1,4,4-trifluorocyclobutene and 3,3,4,4-tetrafluorocyclobutene with high-valency metal fluorides and elemental fluorine were examined. The *vic*-difluorination proceeded mainly in the reactions with CoF_3 and MnF_3 . In contrast, the reaction using AgF_2 proceeded in the different manner, and the unexpected cyclobutenes were formed mainly. And also, the reaction mechanism was discussed.

2. Results and discussion

2.1. Fluorinations of 1,4,4-trifluorocyclobutene

First, the reactions of 1,4,4-trifluorocyclobutene (1) with high-valency metal fluorides and elemental fluorine were examined (Scheme 1 and Table 1). In the reactions with CoF_3 or MnF₃ at 100 °C, the *vic*-difluorination product **2** was a main product along with the further fluorinated products **3–7** (Table 1, Entries 1–4). CoF₃ was more reactive toward **1** than MnF₃. In the reaction with CoF₃ at 100 °C for 3 h, an unexpected product **8** was obtained in 23% yield (Table 1, Entry 1). The reactions using MnF₃ at 150 °C gave **5**

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^{0022-1139/\$ –} see front matter O 2005 Elsevier B.V. All rights reserved. doi:10.1016/j.jfluchem.2005.10.007



Scheme 1. Fluorination of 1,4,4-trifluorocyclobutene with high-valency metal fluoride.

Table 1 Fluorination of 1.4.4-trifluorocyclobutene with high-valency metal fluoride^a

Entry	MF _n	Temperature (°C)	Time (h)	Conv. of 1 (%)	Yield from 1 (%) ^b							
					2	3	4	5	6	7	8	9
1	CoF ₃	100	3	>99	68	2	2	2	0	trace	23	0
2	CoF ₃	100	24	>99	44	13	8	15	6	3	2	2
3	MnF ₃	100	24	57	47	0	0	1	0	0	2	0
4	MnF ₃	100	72	84	70	trace	trace	1	trace	0	2	0
5	MnF ₃	150	6	>99	9	3	trace	55	16	5	0	0
6	AgF_2	100	3	>99	5	0	0	0	0	0	94	trace
7	AgF_2	100	24	>99	9	7	7	trace	10	1	29	30
8	AgF_2	150	1	80	13	0	trace	trace	0	0	63	2
9	CeF ₄	200	1	10	0	0	0	0	0	0	0	0
10	KCoF ₄	200	24	48	25	0	0	0	0	0	14	0
11 ^c	KCoF ₄	200	144	>99	44	0	0	trace	0	0	3	0
12 ^d	F ₂	$-120 \rightarrow rt$	15	71	24	3	3	5	3	trace	trace	0

^a Reaction conditions: 1 (1.0 mmol) and MF_n (10 mmol) were heated in stainless-steel cylinder (volume: 50 ml).

^b Yields were determined by NMR and GC-MS.

^c CH₂FCF₂CF₂CHF₂ was obtained 32% yield.

^d F₂: 1.0 mmol.

as a main product, which was produced by the fluorination of **2** (Table 1, Entry 5). This result means the –CHF– group of **2** was fluorinated easier than –CH₂– group in the case of MnF₃. Employing AgF₂ as a high-valency metal fluoride, the distribution of the products was much different from the results using CoF₃ or MnF₃, and cyclobutenes **8** and **9** were obtained mainly (Table 1, Entries 6–8). The reaction using AgF₂ at 100 °C for 3 h afforded **8** in 94% yield. The reaction using KCoF₄ at 200 °C proceeded very slowly to afford **2**, **8** and CH₂FCF₂CF₂CHF₂ (Table 1, Entries 10 and 11) [13]. CH₂FCF₂CF₂CHF₂ was considered to generate via the ring-opening fluorination of **2**. **2** was obtained in low yield by the reaction with elemental fluorine (Table 1, Entry 12).

2.2. Fluorinations of 3,3,4,4-tetrafluorocyclobutene

Next, the fluorinations of 3,3,4,4-tetrafluorocyclobutene (8) were carried out (Scheme 2 and Table 2). Using CoF₃ and MnF₃ as a high-valency metal fluoride, *vic*-difluorination proceeded to afford **3** (*trans*-isomer) and **4** (*cis*-isomer), and **6** was obtained by the further fluorination of **3** and **4** (Table 2, Entries 1–8). In the reactions with CoF₃ or MnF₃, *trans*-isomer **3** was predominant over *cis*-isomer **4**. Employing AgF₂, **6** was a main product in the reaction at 100 °C for 24 h, while **9** was main product at 100 °C for 1 h (Table 2, Entries 9 and 10). There were two plausible paths

to produce **6**, one is the fluorination of **3** or **4**, and the other is *vic*difluorination of **9**. To consider the results of the reaction for 1 h, the latter might be a predominant one. Using KCoF₄ or CeF₄, **8** was recovered in the reactions at lower than 200 °C, and the complex mixture of products except for **3**, **4**, **6** and **9** were obtained in the reaction at higher temperature (Table 2, Entries 11 and 12). The reaction using elemental fluorine at low temperature gave the similar result to CoF₃ and MnF₃, and the ratio of the isomers **3** and **4** was almost same (Table 2, Entry 13).

2.3. Reaction path and mechanism

In the fluorinations of 1,4,4-trifluorocyclobutene (1) and 3,3,4,4-tetrafluorocyclobutene (8) with high-valency metal fluorides, the unexpected cyclobutenes were obtained especially in the reaction using AgF_2 . At first, the reaction path of the fluorination of 8 would be discussed in Scheme 3, because the reactions of 1 with AgF_2 contained the path of the fluorination of 8.

The *vic*-difluorination (path a) was a predominant and an exclusive path in the case of CoF_3 and MnF_3 , respectively. While, path b to form cyclobutene **9** was predominant in the case of AgF_2 (Scheme 3). The fluorinations of **3** and **4** with CoF_3 , MnF_3 or AgF_2 at the same condition as the fluorinations of **8** did not afford **9**, thus the dehydrofluorination path of **3** and **4** to form **9** was not possible under this condition. The reasonable reaction



Scheme 2. Fluorination of 3,3,4,4-tetrafluorocylcobutene with high-valency metal fluoride.

Table 2 Fluorination of 3,3,4,4-tetrafluorocylcobutene with high-valency metal fluoride^a

Entry	MF_n	Temperature (°C)	Time (h)	Conv. of 8 (%)	Yield from 8 (%) ^b				
					3	4	6	9	
1	CoF ₃	100	1	17	11	5	0	0	
2	CoF ₃	100	24	>99	55	15	22	0	
3	CoF ₃	150	0.25	65	37	25	2	0	
4	CoF ₃	150	1	>99	53	25	17	0	
5	MnF ₃	100	1	27	18	8	0	0	
6	MnF ₃	100	24	>99	56	28	8	0	
7	MnF ₃	150	0.5	42	26	16	0	0	
8	MnF ₃	150	1	>99	54	11	25	0	
9	AgF_2	100	1	77	6	10	22	37	
10	AgF_2	100	24	>99	8	11	73	0	
11	KCoF ₄	250	1	34	0	0	0	0	
12	CeF ₄	250	1	11	0	0	0	0	
13 ^c	F_2	$-120 \rightarrow rt$	24	84	37	33	10	0	

^a Reaction conditions: 8 (1.0 mmol) and MF_n (10 mmol) were heated in stainless-steel cylinder (volume: 50 ml).

^b Yields were determined by NMR and GC-MS.

^c F₂: 1.0 mmol.

mechanism would be proposed in Scheme 4. It had been suggested that the fluorination with a high-valency metal fluoride involves the initial oxidation of the substrate [14]. In the fluorination of **8**, the SET occurred at first, and the generated radical cationic intermediate was quenched by fluoride ion to afford the radical intermediate. This radical was oxidated further by high-valency metal fluoride to afford the cationic intermediate **10**. If **10** was quenched by fluoride ion, **3** and **4** would be obtained. The elimination of proton from **10** would afford **9**.

The reaction path of the fluorination of **1** was summarized in Scheme 5. The *vic*-difluorination (path c) was a predominant path in the case of CoF_3 , MnF_3 , and $KCoF_4$, and path d to from cyclobutene **8** was predominant in the case of AgF_2 . The further fluorination of **8** was same as mentioned above. The plausible mechanism was shown in Scheme 6, which was similar to the mechanism of the fluorination of **8** in Scheme 4.

In both case of the reactions of **1** and **8** with high-valency metal fluoride, the quenching of the cationic intermediate by fluoride ion was predominant in the cases of CoF_3 and MnF_3 , and the elimination of proton from cationic intermediate was predominant in the case of AgF_2 . The reason for the difference had not been clear, however, it was supposed the selectivity depended on the fluorination ability of the radical anion of high-valency metal fluoride, which was counterpart of cationic intermediate.

3. Conclusion

In the fluorination of 1,4,4-trifluorocyclobutene and 3,3,4,4tetrafluorocyclobutene with high-valency metal fluorides such as CoF_3 and MnF_3 , the *vic*-difluorination proceeded mainly. While, the fluorination using AgF_2 proceeded in different manner, and afforded the cyclobutenes mainly. The fluorination with high-valency metal fluorides was considered to be proceeded via the cationic intermediate. The quenching of the cationic intermediate by fluoride ion leading to *vic*difluorination took place mainly in the cases of CoF_3 , MnF_3 and $KCoF_4$. The elimination of proton from the cationic intermediate to form cyclobutene proceeded in the case of AgF_2 .

4. Experimental

4.1. General

High-valency metal fluorides (CoF₃, MnF₃, AgF₂, CeF₄ and KCoF₄) were treated with elemental fluorine at 250 °C for 6 h prior to use. Elemental fluorine was passed through NaF to remove hydrogen fluoride. ¹H (300 MHz) and ¹⁹F NMR (282 MHz) were measured with JEOL ECA-300S using TMS and CFCl₃ as an internal standard and CDCl₃ as a solvent. MS (EI, 70 eV) spectra were measured using the Shimazu GCMS-QP2010 system equipped with GC-2010.

4.2. Preparation of 1,4,4-trifluorocyclobutene (1)

1,4,4-trifluorocyclobutene was prepared by dechlorination of 1,2-dichloro-2,3,3-trifluoroethylene, which was prepared by



Scheme 3. Reaction paths of fluorination of 8.



Scheme 4. Reaction mechanism of fluorination of 8.



Scheme 5. Reaction paths of fluorination of 1.



Scheme 6. Reaction mechanism of fluorination of 1.

cross-coupling cyclobutanation of chlorotrifluoroethylene and vinyl chloride [15].

1,2-dichloro-2,3,3-trifluorocyclobutane (100 mmol), zinc dust (250 mmol) and diethyleneglycol (50 ml) was introduced to a stainless-steel reactor (volume: 150 ml) equipped with a stop valve, and heated at 150 °C. After 12 h, the products were fractionated through traps at -78 and -196 °C with a vacuum

line, and 98.1 mmol (98%) of 1,4,4-trifluorocyclobutene was isolated at a -196 °C trap.

4.3. 1,4,4-Trifluorocyclobutene (1) [16]

¹H NMR: δ 2.63 (2H, m, CH₂), 5.57 (1H, m, CH); ¹⁹F NMR: δ –106.1 (1F, m, CF), –113.7 (2F, m, CF₂). MS: *m*/*z*,

108 (M^+), 89 ($M^+ - F$), 88, 82, 75, 69, 64 ($CF_2CH_2^+$), 58, 57, 39, 31.

4.4. Preparation of 3,3,4,4-tetrafluorocyclobutene (8)

3,3,4,4-Tetrafluorocyclobutene was prepared by dehydrochlorination of 1-chloro-2,2,3,3-tetrafluorocyclobutane [17], which was prepared by cross-coupling cyclobutanation of tetrafluoroethylene and vinyl chloride [12].

1-Chloro-2,2,3,3-tetrafluorocyclobutane (50 mmol), sodium hydroxide (125 mmol) and calcium chloride (50 mmol) were introduced to a stainless-steel reactor (volume: 50 ml) equipped with a stop valve, and heated at 50 °C. After 62 h, the products were fractionated through traps at -60, -120 and -196 °C with a vacuum line, and 45.7 mmol (91% yield) of 3,3,4,4-tetrafluorocyclobutene was isolated at a -120 °C trap.

4.5. 3,3,4,4-Tetrafluorocyclobutene (8) [16,18]

¹H NMR: δ 6.85 (m, CH); ¹⁹F NMR: δ –111.1 (m, CF₂). MS: *m*/*z*, 126 (*M*⁺), 107 (*M*⁺ – F), 100 (CF₂CF₂⁺), 76, 75, 57, 31.

4.6. A typical experimental procedure for the reaction of 1,4,4-trifluorocyclobutene (1) or 3,3,4,4tetrafluorocyclobutene (8) with high-valency metal fluoride (Table 1, Entry 1)

CoF₃ (10 mmol) was placed in a stainless-steel reactor (volume: 50 ml) equipped with a stop valve. **1** (1.0 mmol) was introduced to the reactor at -196 °C with a vacuum line. The reactor was warmed up to 100 °C and stirred for 3 h. After the reaction was completed, the crude products were fractionated through traps at -120 and -196 °C with the vacuum line. The structures and the ratio of the products were determined by GC–MS, ¹H NMR and ¹⁹F NMR spectra.

4.7. A typical experimental procedure for the reaction of 1,4,4-trifluorocyclobutene (1) or 3,3,4,4tetrafluorocyclobutene (8) with elemental fluorine (Table 1, Entry 12)

1 (1.0 mmol) and elemental fluorine (1.0 mmol) was introduced into a stainless-steel reactor (volume: 50 ml) equipped with a stop valve at -196 °C with a vacuum line. The reactor was placed in the ethanol slush (-120 °C), and warmed to ambient temperature gradually for 15 h. After the reaction, products were treated with NaF to remove hydrogen fluoride and fractionated through traps at -120 and -196 °C with the vacuum line. The structures and the ratio of the products were determined by GC–MS, ¹H NMR and ¹⁹F NMR spectra.

4.8. 1,1,2,2,3-Pentafluorocyclobutane (2)

¹H NMR: δ 2.86 (2H, m, CH₂), 5.09 (1H, d of m, J = 52.6 Hz, CHF); ¹⁹F NMR: δ -113.6 (1F, d of m, J = 216.9 Hz, CF₂), -115.9 (1F, d of m, J = 216.9 Hz, CF₂),

-118.6 (1F, d of m, J = 220.1 Hz, CF₂), -135.1 (1F, d of m, J = 220.1 Hz, CF₂), -202.6 (1F, d of m, J = 52.6 Hz, CHF). MS: m/z, 100 (CF₂CF₂⁺), 95, 82 (CF₂CHF⁺), 77, 75, 69, 64 (CF₂CH₂⁺), 57, 51, 46 (CHFCH₂⁺), 31.

4.9. Trans-1,1,2,2,3,4-hexafluorocyclobutane (3) [19]

¹H NMR: δ 5.25 (d of m, J = 47.6 Hz, CHF); ¹⁹F NMR: δ -122.0 (2F, d of m, J = 230.0 Hz, CF₂), -134.3 (2F, d of m, J = 230.0 Hz, CF₂), -208.6 (2F, d of m, J = 47.6 Hz, CHF). MS: m/z, 100 (CF₂CF₂⁺), 95, 82 (CF₂CHF⁺), 69, 64 (CHFCHF⁺), 51, 31.

4.10. Cis-1,1,2,2,3,4-hexafluorocyclobutane (4)

¹H NMR: δ 5.13 (m, CHF); ¹⁹F NMR: δ –119.4 (2F, d of m, J = 235.1 Hz, CF₂), –134.0 (2F, d of m, J = 235.1 Hz, CF₂), –223.8 (2F, m, CHF). MS: m/z, 100 (CF₂CF₂⁺), 95, 82 (CF₂CHF⁺), 69, 64 (CHFCHF⁺), 51, 31.

4.11. 1,1,2,2,3,3-Hexafluorocyclobutane (5)

¹H NMR: δ 3.15 (quin of t, J = 12.0 Hz, 3.7 Hz, CH₂); ¹⁹F NMR: δ -117.6 (4F, t, J = 12.0 Hz, CF₂CH₂), -131.5 (2F, t, J = 3.7 Hz, CF₂CF₂CF₂). MS: m/z, 145 ($M^+ -$ F), 100 (CF₂CF₂⁻⁺), 95, 75, 69, 64 (CF₂CH₂⁻⁺), 50, 31.

4.12. 1,1,2,2,3,3,4-Heptafluorocyclobutane (6)

¹H NMR: δ 5.31 (m, CHF); ¹⁹F NMR: δ –123.3 (2F, d of m, J = 234.4 Hz, CF₂), -130.7 (1F, d of m, J = 231.0 Hz, CF₂), -134.9 (1F, d of m, J = 231.0 Hz, CF₂), -136.2 (2F, d of m, J = 234.4 Hz, CF₂), -218.6 (1F, d of m, J = 48.4 Hz, CHF). MS: m/z, 131, 113, 100 (CF₂CF₂⁺), 93, 82 (CF₂CHF⁺), 75, 69, 51, 31.

4.13. Perfluorocyclobutane (7) [20,21]

¹⁹F NMR: δ –134.0 (s, CF₂). MS: *m*/*z*, 131, 100 (CF₂CF₂⁺), 93, 69, 50, 31.

4.14. 2,3,3,4,4-Pentafluorocyclobutene (9)

¹H NMR: δ 5.93 (m, CH); ¹⁹F NMR: δ –104.2 (1F, m, CF), –113.7 (2F, m, CF₂), –118.4 (2F, m, CF₂). MS: *m*/*z*, 144 (*M*⁺), 125 (*M*⁺ – F), 100 (CF₂CF₂⁺), 94, 93, 75, 69, 31.

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