Synthesis of Versatile Poly- and Perfluorinated Compounds by Utilizing Direct Fluorination, 1

A New Route to Perfluoro(Propyl Vinyl Ether) Monomer: Synthesis of Perfluoro(2-propoxypropionyl) Fluoride from Non-Fluorinated Compounds

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Dedicated to Professor Richard D. Chambers on the occasion of his retirement.

Abstract: Perfluoro(2-propoxypropionyl) fluoride (**1 a**), which is the precursor of the perfluorinated propyl vinyl ether (PPVE) monomer of an industrially important perfluoroalkoxy copolymer (PFA), was synthesized by utilizing direct fluorination of the non-fluorinated counterpart for the first time. The partially-fluorinated ester **7** synthesized from the desired perfluorinated acid fluoride **1 a** itself and the non-fluorinated alcohol **5**, which has a carbon skeleton corresponding to the desired compound **1 a**, was perfluorinated by liquid-phase direct fluorination with elemental fluorine. Degradation of the resulting perfluorinated ester **8** gave 2 mols of the desired acid fluoride **1 a**. In a sense, this process can be called self-multiplication of a perfluorinated acid fluoride from a non-fluorinated alcohol.

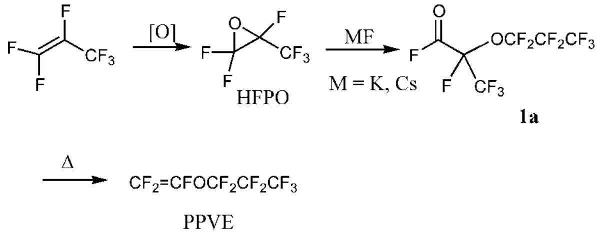
Keywords: acyl fluorides; direct fluorination; fluorine; perfluoropolymers; perfluoro(propyl vinyl ether); synthesis design

Introduction

Perfluoroalkoxy copolymer [PFA: copolymer of tetrafluoroethylene (TFE) and perfluoro(propyl vinyl ether) (PPVE)] is one of the most important perfluorinated polymers that is used both as a thermally and chemically resistant material for industrial purposes, and especially in recent medical, IT and electronics applications.[1,2] However, it has disadvantages in that it is expensive because so far, it has been prepared from hexafluoropropylene oxide (HFPO), which is itself very costly (Scheme 1).[3]

Recently, use of perfluorinated hypofluorite chemistry[4] was reported to lead to an improved process. Also, the synthesis of perfluoro(alkyl vinyl ethers) by direct fluorination of partially fluorinated 1,2-dichloroethyl ethers has been reported.[5] However, these syntheses still require expensive (per)fluorinated starting materials.

Herein we present an essentially different approach. Our new synthetic route to PPVE starts from a non-fluorinated counterpart and utilizes liquid-phase direct fluorination[6] as a key step (Scheme 4) and, therefore, solves this long-standing problem. The desired perfluorinated acyl fluoride **1 a**, the precursor of PPVE, can be multiplicated by supplying the non-fluorinated alcohol **5** with a carbon skeleton corresponding to that of the desired product **1 a**. The essential raw materials of this process are only the non-fluorinated alcohol **5** and fluorine gas, although it still requires the perfluoroacyl fluoride **1 a** itself for the first cycle.



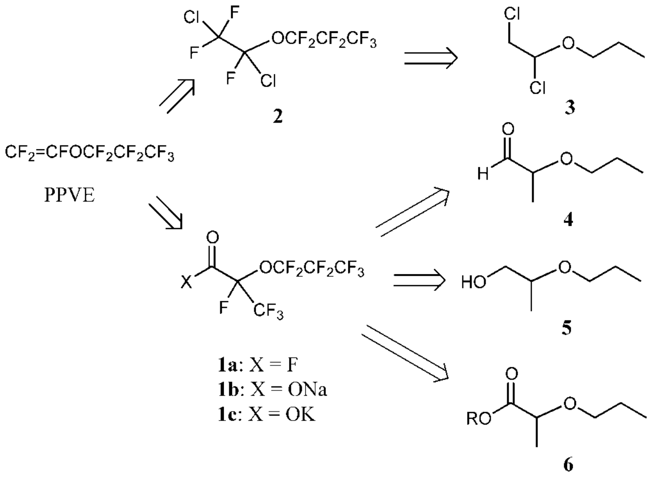
Scheme 1. Conventional synthesis of PPVE.

Results and Discussion

In 1989, Lagow et al. reported liquid-phase direct fluorination of non-fluorinated compounds.[6] Although they only applied this process to molecules with simple structures such as octyl octanoate, we considered that it could also be applicable to the synthesis of industrially important compounds such as perfluorinated alkyl vinyl ethers providing that we could make the corresponding hydrocarbon counterparts. From such a point of view, we reconsidered the design of the synthesis of PPVE retrosynthetically (Scheme 2).

PPVE could be made either by dechlorination of perfluorinated dichloroether **2** (Route I)[4,5] or by thermal elimination of perfluorocarboxylic acid derivatives **1 a–c** (Route II)[3]. Compound **2** could be obtained by direct fluorination of the corresponding hydrocarbon dichloroether **3**. The perfluoroacyl fluoride **1 a** could be derived from aldehyde **4**, where all fluorine atoms are substituted by hydrogen atoms. Alcohol **5** could also be a precursor to acid fluoride **1 a** because its perfluorinated derivative would lead to the desired compound **1 a**. Alkali salts, **1 b** and **1 c**, of the perfluorocarboxylic acid could be derived from the acid fluoride **1 a**.

Among these candidates, compound **3** seemed, at first sight, to be the best, because it could be obtained from inexpensive propyl vinyl ether in only one step. Therefore, we chose Route I for our first trial.



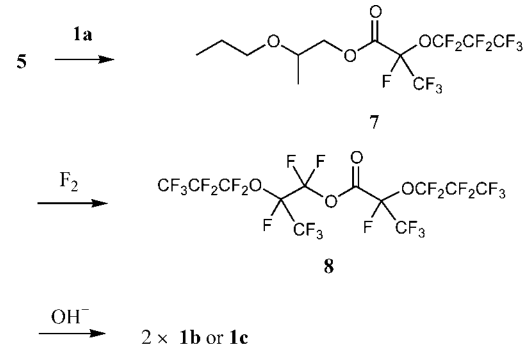
Scheme 2. Retrosynthetic analysis of PPVE.

Chlorination of propyl vinyl ether was conducted according to a literature procedure[7] to give dichloroether **3** in 75% yield. The chlorination was relatively difficult because of the formation of a trichloro derivative. Besides, it was difficult to purify the dichloroether **3** by distillation or even by chromatography due to its instability. Thus, direct fluorination without purification of the substrate was carried out, basically applying Lagow's method. The direct fluorination was conducted with 20% F_2/N_2 and proceeded as we had intended, but the yield was only 40% at best and it was limited by migration of chlorine atoms. Furthermore, considerable amounts of products arising from C–C and C–O bond cleavage were formed during fluorination, probably because of some reaction in the vapor phase. This suggested that the substrate **3** was too volatile to be fluorinated in this way.

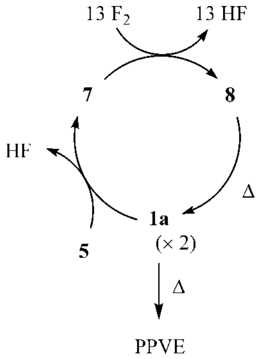
We then returned to the retrosynthesis shown in Scheme 2 and decided to examine Route II. There were three possible precursors as mentioned above. Among them, compound **5** was chosen because it could be easily prepared. However, direct fluorination of it seemed to be dangerous because formation of an unstable hypofluorite would be likely to occur first.[8] Protection of the OH group was essential in this route.

The protecting group in this case should be a perfluorinated group in order to moderate the reactivity towards fluorination, it should also be of large molecular weight for low volatility, and it should be removable after fluorination. Considering these demands, $–COCF(CF_3)OCF_2CF_2CF_3$ seemed to be most attractive because it could be removed by alkaline hydrolysis after fluorination to give the same component, **1 b** or **1 c**, as that from the hydrocarbon moiety after perfluorination (Scheme 3). Besides, this protecting agent is available as the acid fluoride **1a**, which is an intermediate to PPVE in the conventional manufacturing process.

At the time when the study of this method started, Lagow et al. reported that thermal decomposition of



Scheme 3. Use of 1a as a protecting agent.



Scheme 4. The "PERFECT" process.

a perfluoroester gave 2 mols of perfluoroacyl fluorides.[9] For example, thermal decomposition of perfluoro(octyl octanoate) gave 2 mols of perfluorooctanoyl fluoride. This indicated that the acyl fluoride **1 a** could be recyclable, by adopting it to our process.

Scheme 4 shows our new methodology. The non-fluorinated alcohol **5** is esterified with the desired perfluoroacyl fluoride **1 a**, before doing the direct fluorination. Then, liquid-phase direct fluorination of the obtained partially-fluorinated ester **7** gives the perfluorinated ester **8**. Thermal elimination of **8** gives 2 mols of the desired acyl fluoride **1 a**. The obtained acyl fluoride can be used either for the next cycle of the production or for further thermal elimination to PPVE. We named this process "PERFECT" that is the abbreviation of PERFluorination of an Esterified Compound then Thermal elimination.

The actual synthesis was carried out as follows: The starting, non-fluorinated alcohol, 2-propoxy-1-propanol (**5**), was synthesized from inexpensive propylene oxide and 1-propanol in one step.[10] Although the reaction gave a mixture of regioisomers in ca. 1 : 1 ratio, it was possible to separate them by distillation, and the isomer, 1-propoxy-2-propanol, could be used as a commercial detergent.

Esterification, direct fluorination, and thermal degradation to compound **1 a** were achieved in 99%, 93%, and 94% yield, respectively. Further thermal degradation to PPVE from **1 a** is a well known process.[3]

Esterification was carried out simply by mixing the non-fluorinated alcohol **5** with the perfluoroacyl fluoride **1 a** and removing the HF formed during the reaction, out of the reaction system, in a stream of nitrogen.

The next liquid-phase direct fluorination was carried out basically in manner similar to Lagow's method. However, by employing the higher-molecular weight, partially-fluorinated ester **7** as the substrate, any dangerous vapor-phase reactions can be avoided and the solubility of the substrate in the solvent used in the liquid-phase fluorination, i. e., 1,1,2-trichlorotrifluoroethane or even compound **1 a** itself, can be improved. This is in contrast to the solubility of a non-fluorinated compound.[11] As described in the literature[6,11b], the appropriate dilution of fluorine, the appropriate dilution of the substrate in an inert solvent, and use of an excess amount of fluorine to replace all of the hydrogen atoms in the substrate at all times are essential. In order to achieve this, the continuous feed of both diluted fluorine gas and the substrate in perfluorinated solvent at a controlled rate with a molar ratio $F_2/H = 2.8$ was carried out. Injection of a dilute solution of benzene after adding the substrate was effective for complete perfluorination, because benzene reacts with elemental fluorine to generate a lot of fresh fluorine radicals.[6] The total reaction time was quite long in laboratory scale experiments, because it depends on the flow rate of fluorine gas. Manufacturing efficiency would be better on a larger scale, because a large amount of fluorine gas can be generated in a factory.

The following thermal elimination step was carried out either in the vapor phase without catalyst, or in the liquid phase with a catalytic amount of alkali fluoride, as described in the literature[9,12]. For example, liquid-phase reaction with 30 mol % of sodium fluoride gave the desired product **1 a** in excellent yield.

By repeating the cycle shown in Scheme 4, the amount of perfluoro(2-propoxypropionyl) fluoride (**1 a**) will increase in geometric progression. For the case of perfluoro(propyl vinyl ether), the overall yield of the product **1 a** based on the starting perfluoroacyl fluoride **1 a** was 170% for one cycle so that we will, in theory, get 1.7^n times as much **1 a** as we start with, after n times repeating of the cycle. In that sense, the cycle shown in Scheme 4 is a self-multiplication process.

Further studies on application to other perfluorinated compounds using the above described synthetic method are now under investigation.

Conclusions

The synthetic method utilizing liquid-phase direct fluorination with elemental fluorine for the industrially important perfluoromonomer PPVE was investigated. Direct fluorination of dichloroether **3** did not give a good yield. Moreover, this was not practical, because the compound has high volatility allowing vigorous reaction and consequent bond cleavage in the vapor phase and it has a low solubility in the solvent used in the direct fluorination. On the other hand, direct fluorination of the partially fluorinated ester **7**, synthesized from non-fluorinated alcohol **5** and the desired perfluorinated acid fluoride **1 a** itself, was achieved in high yield. Degradation of the resulting ester **8** gave 2 mols of the desired acid fluoride **1 a** (Scheme 4).

The substrate in this liquid-phase direct fluorination is a partially-fluorinated ester, which is obtained by simple organic synthesis directly from a hydrocarbon precursor, and therefore has advantages over other known direct fluorination methods as follows.

1. It avoids vapor-phase reaction by employing a substrate which has a low vapor pressure.

2. It significantly increases the solubility of the substrate in the perfluorinated solvent used for fluorination, compared to non-fluorinated ester.

3. It is easy to synthesize the partially-fluorinated substrate because perfluorinated acyl fluoride **1 a** is available from the conventional manufacturing process and then from self-multiplication.

The raw materials are inexpensive propylene oxide, 1-propanol, and fluorine gas, and it is possible to recycle the hydrogen fluoride evolved during the reactions to generate fluorine gas. Therefore, this method can reduce the manufacturing cost of PPVE.

Experimental Section

General Remarks

NMR spectra were obtained on a JEOL EX-400 or α-600 (tetramethylsilane as internal standard for ^{1}H, trichlorofluoromethane for ^{19}F, and $CDCl_3$ for ^{13}C). High resolution mass spectra were obtained on JEOL SX-102A coupled to HP-5890 with a 60-m capillary column, J & W DB-1.[13] Elemental fluorine was generated by Fluoro Gas Fluorodec 30. *Elemental fluorine is highly toxic and corrosive gas, and may cause explosions when it meets organics in the vapor-phase. Extreme care must be taken when handling it! Both the liquid and vapor of hydrogen fluoride (bp: 19.5 °C) evolved during the reaction are also highly corrosive and cause severe burns upon contact. Care must be taken! Prior to use, all hydrocarbon greases must be removed and the apparatus must be gradually passivated with elemental fluorine.* Although the use of 1,1,2-trichlorotrifluoroethane (CFC-113) is subject to environmental regulatations, we will mention experimental examples with it for convenience, because it is still much more cheaply available (Aldrich) than compound **1a** for use as solvent. *Care must be taken in order to avoid discharge to the environment.* Once enough of the compound **1 a** is obtained in the cycle, it should be used instead of CFC-113. Other reagents were obtained from Kanto Chemicals and used without purification.

Perfluorodichloroether (2)

Ref. [5]: In a 2-L autoclave made of hastelloy C, equipped with a condenser maintained at –10 °C at the gas outlet of the autoclave, a suspension of sodium fluoride (60.0 g, 1.43 mol) and 1,1,2-trichlorotrifluoroethane (1290 g) was stirred and maintained at –10 °C. Nitrogen gas was blown into the system for 1.5 hours, and then, fluorine gas diluted to 20% with nitrogen gas, was blown into the mixture for 1 hour at a flow rate of 12.5 L/h at atmospheric pressure. While blowing the 20% fluorine/nitrogen at the same rate, a solution of dichlorovinyl propyl ether **3**[7] (20.0 g, 0.127 mol) dissolved in 1,1,2-trichlorotrifluoroethane (394 g) was injected over a period of 18 hours. Then, while blowing the 20% fluorine/nitrogen at the same rate, a solution of benzene in 1,1,2-trichlorotrifluoroethane (0.01 g/mL) was injected in an amount of 12 mL while raising the temperature from –10 °C to room temperature. Then, the inlet for benzene injection was closed, and the outlet valve of the autoclave was closed. When the pressure reached 0.12 MPa, the fluorine gas inlet valve of the autoclave was closed, and stirring was continued for 1 hour. During this time, the pressure dropped slightly. Then the pressure was adjusted to atmospheric pressure, and while maintaining the internal temperature of the reactor at room temperature, another benzene solution (12 mL) was injected, and the same operation was repeated five times. The total amount of benzene injected was 0.74 g. Further nitrogen gas was blown into the mixture for 4.5 hours. The yield was determined by NMR with perfluorobenzene as an internal standard to be 40%.

Partially-Fluorinated Ester (7)

In a 2-L autoclave made of hastelloy C, acyl fluoride **1a** (1800 g, 5.43 mol) was added dropwise to distilled 2-propoxy-1-propanol (620 g, 5.25 mol) over a period of 8 hours while bubbling nitrogen gas to strip off hydrogen fluoride evolved, and maintaining the internal temperature between 25 and 35 °C. After the addition, stripping off remaining HF and excess acyl fluoride **1 a** by bubbling nitrogen gas gave partially fluorinated ester **7**; yield: 2245 g (5.22 mol, 99.2%); bp 52–61 °C/3.6–4.0 kPa; ^{1}H NMR (399.8 MHz, $CDCl_3$): $\delta = 0.90$ (t, $J = 7.5$ Hz, 3 H), 1.20 (d, $J = 5.4$ Hz, 3 H), 1.50–1.60 (m, 2 H), 3.33–3.50 (m, 2 H), 3.64–3.74 (m, 1 H), 4.23–4.29 (m, 1 H), 4.34–4.41(m, 1 H); ^{19}F NMR (376.2 MHz, $CDCl_3$): $\delta =$ –80.9 and –87.4 (2 F, AB quartet, $J_{FF} = 149$ Hz), –82.3 (3F), –83.1 (3 F), –130.7 (2 F), –132.7 (1 F); high resolution mass spectrum (EI method): $m/z = 431.0746$ (M + H, calculated for $C_{12}H_{14}F_{11}O_4$: 431.0716).

Perfluorinated Ester (8)

In a 3-L autoclave made of nickel, equipped with a condenser maintained at 20 °C, an NaF pellet packed layer, and condenser maintained at –10 °C in series at the gas outlet of the autoclave, as well as a liquid returning line in order to return the condensed liquid from the condenser maintained at –10 °C, 1,1,2-trichlorotrifluoroethane (1890 g) was stirred and maintained at 25 °C. Nitrogen gas was blown into the system for 1.5 hours, and then, fluorine gas diluted to 20% with nitrogen gas, was blown into the mixture for 3 hours at a flow rate of 8.91 L/h at atmospheric pressure. While blowing the 20% fluorine/nitrogen at the same rate, a solution of partially-fluorinated ester **7** (60.0 g, 0.139 mol) dissolved in 1,1,2-trichlorotrifluoroethane (601 g) was injected over a period of 63.7 hours. Then, while blowing the 20% fluorine/nitrogen at the same rate, a solution of benzene in 1,1,2-trichlorotrifluoroethane (0.01 g/mL) was injected in an amount of 18 mL while raising the temperature from 25 °C to 40 °C. Then, the inlet for benzene injection was closed, and the outlet valve of the autoclave was closed. When the pressure reached 0.20 MPa, the fluorine gas inlet valve of the autoclave was closed, and stirring was continued for

1 hour. During this time, the pressure dropped slightly. Then the pressure was adjusted to atmospheric pressure, and while maintaining the internal temperature of the reactor at 40 °C, another portion of benzene solution (6 mL) was injected, and the same operation was repeated twice. The total amount of benzene injected was 0.309 g. Further nitrogen gas was blown into the mixture for 2.0 hours. Distillation gave the perfluorinated ester **8**; yield: 86.0 g (0.129 mol, 93.2%); bp. 46–51 °C/5.2 kPa; ^{19}F NMR (564.6 MHz, $CDCl_3$/C_6F_6): $\delta = -80.6$ (1F), –80.8 and –80.9 (3 F), –81.6 to –83.1 (2 F), –82.6 (6 F), –82.8 (3 F), –86.7 (1 F), –87.4 (1 F), –87.5 (1 F), –130.6 (4 F), –132.2 (1 F), –145.7 and –145.9 (1 F); ^{13}C NMR (150.8 MHz, $CDCl_3/C_6F_6$): $\delta = 100.26$ and 100.28, 102.8, 106.8, 107.0, 116.0, 116.2, 116.5 and 116.6, 117.4, 117.5, 117.9, 117.9, 152.2 and 152.3; high resolution mass spectrum (CI method): 664.9496 (M + H, calculated for $C_{12}HF_{24}O_4$: 664.9492).

Degradation of Perfluorinated Ester (8)

In a 100-mL flask with reflux condenser adjusted at 70 °C, a suspension of perfluorinated ester **8** (55.3 g, 83.2 mmol) and NaF powder (0.70 g, 17 mmol) was heated at 140 °C for 15 hours in an oil bath with vigorous stirring. A liquid sample (52.1 g, 157 mmol, 94.2% yield) was recovered through the condenser. It corresponded with the authentic compound **1 a**[14] both by gas chromatography and NMR.

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