A synthetic method for the production of perfluorinated building blocks

The "perfect" direct fluorination technique

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ABSTRACT: Perfluorinated compounds play an important role in the materials industry, although perfluorinated building blocks have not been widely available for very long. The recent development of liquid-phase direct fluorination techniques has brought about the production of various new perfluorinated compounds. The methods for preparing perfluorinated compounds are reviewed, and recent developments in techniques for the synthesis of perfluorinated building blocks are presented.

INTRODUCTION

Perfluorinated compounds are important components in industrial materials such as the both thermally and chemically resistant materials used in modern medical and electronics applications (1). The outstanding resistance to corrosive chemicals is derived from the high stability of the C-F bonds. This makes perfluorinated building blocks also attractive in the pharmaceutical and agricultural fields, since the C-F bond in the fluorinated molecule resists metabolism, which has various biological effects. However, perfluorinated building blocks are not widely available. Actually, most fluorinated materials consist of $-CF_2CF_2-$, $-CF_2CF(CF_3)-$, $CF_3(CF_2CF_2)_n-$, $CF_3CF_2CF_2O-$, and $CF_3C(=O)-$ as the perfluorinated building blocks. This is primarily because there are only a few precursors available to generate the perfluorinated building blocks, in turn because the synthesis of perfluorinated compounds has been quite limited.

From a synthetic viewpoint, there are two approaches to synthesizing organofluorine compounds. One is to introduce fluorine directly into the target molecules (the fluorination method). The other is to synthesize the target molecules via the reaction of fluorinated compounds of low molecular weight (the building block method). In general, the building block method is adopted to produce perfluorinated compounds. However, the reactivity of substrates and reagents commonly changes drastically when fluorine atoms are introduced into the reactive sites of the molecule (2). This tendency becomes more severe when the number of fluorine atoms increases. Of course, the synthesis of the perfluorinated building blocks themselves via the fluorination approach has been attempted, although this process has also been very difficult (3). However, this method does not experience difficulty in the construction of the backbone structure, because it can utilize non-fluorinated substrates that are accessible by common organic synthesis.

This work is focused on the synthetic methods for constructing perfluorinated building blocks by direct fluorination from C-H to C-F.

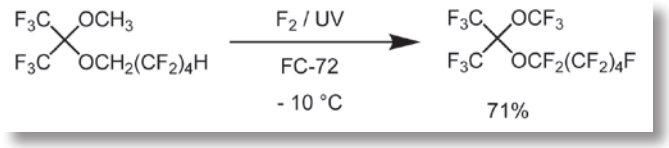
The PERFECT method can provide various perfluorinated building blocks

FLUORINATION USING COBALT TRIFLUORIDE

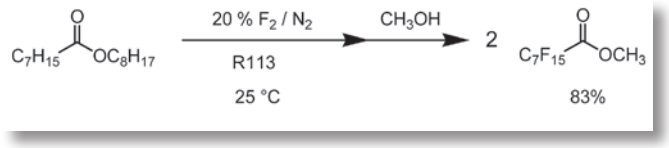
During World War II, an inert liquid was required for the treatment of UF_6. The fluorination of C-H bonds in a hydrocarbon with CoF_3 at high temperature was developed for this purpose. After World War II, this technique was utilized for the production of low molecular weight fluorocarbon fluids (4). However, this method is not suitable for the synthesis of perfluorinated compounds having functional group(s). This means that fluorination using CoF_3 does not provide a synthetic route to perfluorinated building blocks.

FLUORINATION BY ELECTROCHEMICAL METHODS

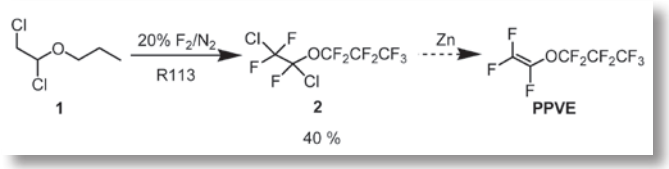
The electrochemical fluorination (ECF) process was invented during World War II. In this method, the fluorination of C-H bonds is achieved by means of an electrode reaction in anhydrous hydrogen fluoride (5). After World War II, this technique was improved upon and has been applied for inert fluids, textile finishes and oil repellent agents ever since. This method can be adapted to the synthesis of perfluorinated derivatives possessing functional groups such as perfluoroethers, perfluoroamines, perfluoroacyl fluorides, and perfluoroalkanesulfonyl fluorides. Perfluoroacyl fluorides can be reacted with nucleophiles or be reduced to alcohols which react with electrophiles. This means that ECF provides a preparative method for perfluorinated building blocks. However, it has the drawbacks of low productivity and poor yield (6).



Scheme 1. A representative direct perfluorination by SYO-LPDPF.



Scheme 2. A representative direct perfluorination by Exfluor-Lagow method.



Scheme 3. Synthesis of a precursor to PPVE by Exfluor-Lagow method.

DIRECT FLUORINATION WITH ELEMENTAL FLUORINE

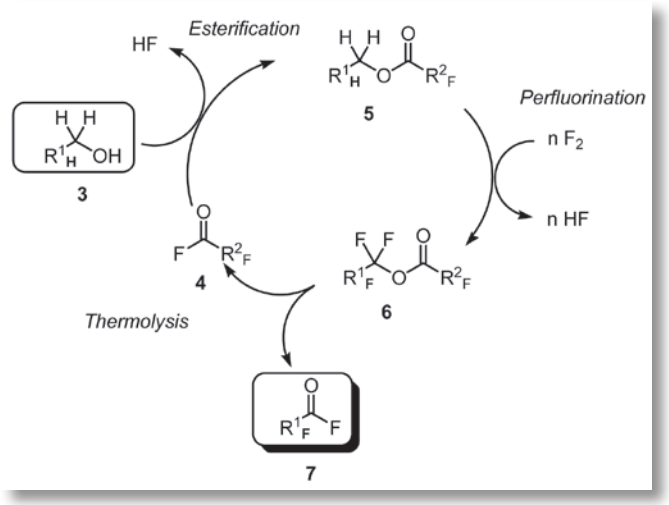
Direct fluorination using F_2 has been studied ever since elemental fluorine was isolated by Moissan. Until the 1980's, it was very difficult to control the violent nature of the reaction (1, 3). The gas-phase reaction (jet fluorination) was applicable only to low molecular weight hydrocarbons lacking functional groups. The solid-phase reaction (LaMar method) had a wider scope, but was quite sophisticated and unsuitable for the industrial scale production of perfluorinated compounds.

A breakthrough was brought about by Scherer, Yamanouchi, and Ono (7). They discovered a practical liquid-phase direct perfluorination method (Scherer-Yamanouchi-Ono Liquid-Phase Direct PerFluorination, SYO-LPDPF) through a study of artificial blood substitutes. The method is quite unique in its inverse addition of a substrate into an inert liquid saturated with concentrated fluorine gas under UV irradiation (Scheme 1). The inverse addition requires a large excess of F_2 relative to the number of hydrogen atoms to be replaced in the substrate. This technique enabled the reaction to proceed under mild conditions. However, the substrates are restricted to partially fluorinated ones which have sufficient solubility in a perfluoroalkane solvent such as FC-72 (C_6F_{14}). Nonetheless, partially fluorinated substrates are more stable towards the fluorination process than the corresponding non-fluorinated compounds. Perfluoro ethers were prepared by the direct fluorination of partially fluorinated substrates (8).

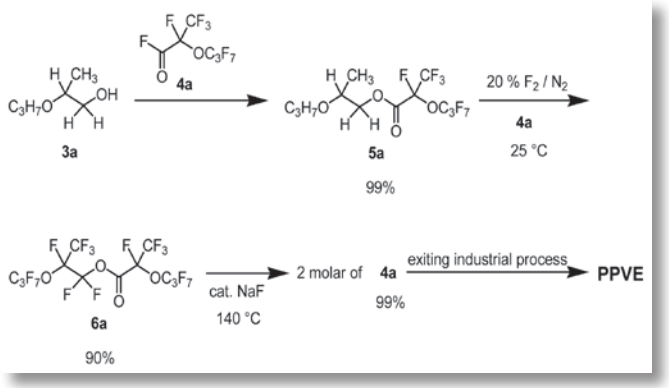
This concept was expanded upon by Lagow et al. with their elemental fluorine process (Exfluor-Lagow method). They employed the same inverse addition, but with diluted fluorine and without UV irradiation, in a chlorofluorocarbon (CFC) such as R113 (CCl_2FCClF_2) (Scheme 2) (9). This method yields various perfluorinated products via the direct fluorination of non-fluorinated compounds in high yields (the perfluorinated product was isolated as the methyl ester after methanolysis in this case). It can also provide perfluorinated compounds which possess functional group(s) such as perfluoroesters, perfluoroacyl fluorides and perfluoroketones, which can react further with other reagents.

Therefore, it is a powerful tool for the construction of

It does not use any solvent other than the perfluoroacyl fluoride which is either a product or the intermediate in the process



Scheme 4. The PERFECT process for a perfluorinated acyl fluoride.



Scheme 5. Synthesis of the industrial precursor of PPVE by the PERFECT process.

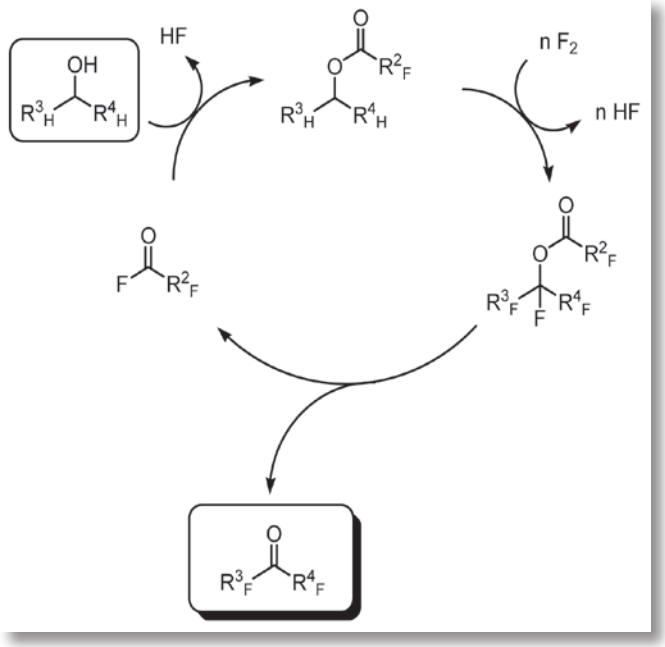
perfluorinated building blocks. A drawback is that it employs a CFC, regulated in use for environmental reasons, as the solvent.

A "PERFECT" DIRECT FLUORINATION TECHNIQUE

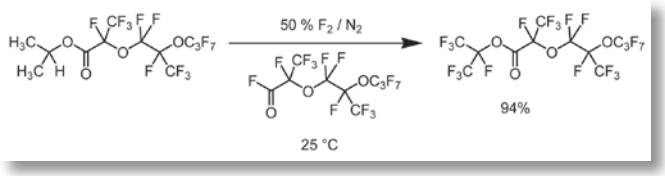
Okazoe et al. attempted the direct application of the Exfluor-Lagow method to a small molecule, such as a precursor **2** of perfluoro propyl vinyl ether (PPVE), the monomer of perfluoroalkoxy copolymer (PFA) (Scheme 3) (10). However, it was difficult to obtain **2** in high yield, because of some indeterminate reaction which took place in the vapour phase, presumably due to the volatility of the small substrate **1**, and which led to an explosion in some cases.

In order to solve this problem, they developed the "PERFECT" process (Scheme 4) (10). The name is an acronym for the PERFluorination of an Esterified Compound, then Thermolysis. By employing a higher-molecular weight, partially-fluorinated ester **5**, which is synthesized from a non-fluorinated alcohol **3** and a perfluorinated acyl fluoride **4**, as the substrate for the direct fluorination, any dangerous vapour-phase reactions can be avoided. The direct fluorination of **5** with elemental fluorine by the inverse addition gave the desired perfluorinated ester **6**. Thermolysis of **6** in the presence of catalytic amount of sodium fluoride gave the desired perfluorinated compound **7** and returned the acyl fluoride **4**.

In the synthesis of the precursor to PPVE, perfluorination proceeded in 90 percent yield and the process gave 2 molar equivalents of **4a**, which is used to produce PPVE via the existing industrial process (Scheme 5). The perfluoroacyl fluoride **4a** serves as the precursor for PPVE as well as the



Scheme 6. The PERFECT process for a perfluorinated ketone.



Scheme 7. A representative direct perfluorination by the PERFECT process.

perfluoroacylating agent in this case. This process provides various perfluoroacyl fluorides for use as novel perfluorinated building blocks (11) and as the monomers in an ion exchange membrane (12). Polymers were also applied as the substrates (13).

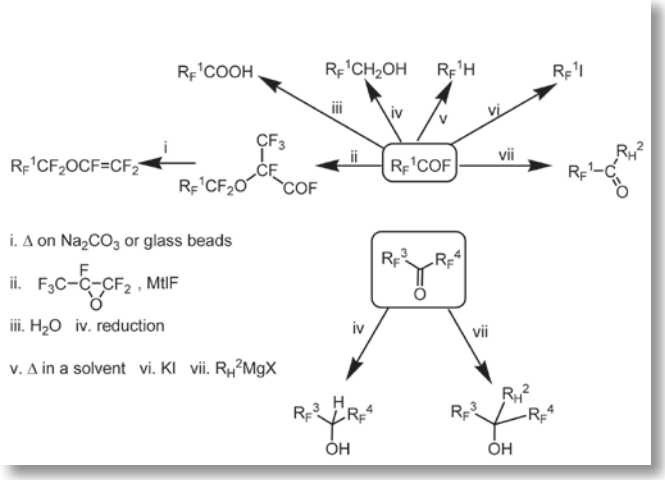
When a secondary alcohol is employed as the non-fluorinated starting material, the corresponding perfluorinated ketone is obtained (Schemes 6 and 7) (14).

The PERFECT method takes advantage of the merits of direct fluorination; that is, the only byproduct of the process is hydrogen, theoretically, because the hydrogen fluoride which is formed in the process can be converted electrochemically back to hydrogen and fluorine, and the fluorine can then be used again in the process.

Moreover, this methodology has advantages over other direct fluorination methods as follows: First, it avoids a dangerous vapour-phase reaction by employing a substrate with a lower vapour pressure. Second, it makes synthesizing the partially-fluorinated substrate easier, because perfluorinated acyl fluorides are available via a conventional manufacturing process. And finally, it does not use any solvent other than the perfluoroacyl fluoride which is either a product or the intermediate in the process.

Thus, the PERFECT method can provide various perfluorinated building blocks, examples of which are shown in Scheme 8.

By using the PERFECT method, a new fluorinated surfactant and a new lubricant for hard disk drives have been produced industrially. The new fluorinated surfactant is an alternative to ammonium perfluorooctanoate (APFO: the surfactant which is broadly used in fluoropolymer industries but shows bioaccumulation in the environment). Thus, the method contributes to reduce the environmental impact of the field.



Scheme 8. Building blocks from the PERFECT products.

CONCLUSIONS

Various perfluorinated building blocks have come to be available by the development of liquid phase direct perfluorination using elemental fluorine. In particular, the PERFECT method can provide perfluorinated carboxylic acid derivatives and perflorinated ketones of widely varying molecular weight.

Thus, the method serves to generate various perfluorinated building blocks which are useful in the pharmaceutical and agricultural fields.

Moreover, it does not require any solvent other than the product itself or intermediates of the process.

In that sense, it contributes to reduce the environmental burden associated with the production of industrial perfluorinated chemicals.

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