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Persistent fluorocarbon radicals generated by elemental and electrochemical fluorination

Udo Groß *, Stephan Rüdiger, Anton Dimitrov

Institut für Anorganische und Analytische Chemie der Freien Universität Berlin, Fabeckstr. 34-36, 14195 Berlin, Germany

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Abstract

Stable fluorocarbon radicals were obtained by fluorination of branched fluoro-olefins and unsaturated partially fluorinated tertiary amines. As a fluorine source, elemental fluorine as well as the electrochemical fluorination process (ECF) in anhydrous hydrogen fluoride (AHF) were used. The persistent radicals were investigated by ESR spectroscopy concerning their structure and stability. ECF-generated fluorocarbon radicals give some evidence of intermediately formed atomic fluorine as a key factor of the AHF-based electrochemical process. These findings favour an electrofluorination mechanism similar to that of elemental fluorine.

Because of their unusual stability, the radicals can be used as spin markers and to obtain 2D images by using an ESR tomographic technique. Stabilized with emulsifiers, they form stable aqueous emulsions.

Keywords: Fluorocarbon radicals; Elemental fluorination; Electrochemical fluorination; Branched fluoro-olefins; Partiallly fluorinated tertiary amines; ESR spectroscopy

1. Introduction

A few strongly branched perfluorinated olefins are known to give stable perfluorinated radicals when treated with elemental fluorine [1,2]. The well-documented standard example is based on *F*-2,4-dimethyl-3-ethyl-2-pentene, which is transformed in high concentration to the sterically hindered free radical by fluorination [1]. Instead of gaseous fluorine, Russian researchers used γ-radiolysis of solid and liquid fluorocarbons to generate paramagnetic centres with different stabilities [3].

We have successfully applied the partial fluorination of the double bond to branched unsaturated compounds and also to amino and ether derivatives of the corresponding *F*-olefins. In addition, fluorination products of tertiary amines of the electrochemical fluorination process were investigated by ESR, exhibiting evidence of formed fluorinated radicals [4]. From this, conclusions were drawn to contribute to controversal discussions of the ECF mechanism.

2. Experimental details

The fluoro-olefins **1** and **7** (see Table 1) and the non-tabulated hexafluoropropene (HFP) trimer, C_9F_{18}, as well as the perfluoro-1,4-dimethylbenzene were commercial products with a purity greater than 95%. The HFP trimer derivatives **2** and **3** were prepared as described in Ref. [5] and in the reference cited therein. Compound **4** was obtained by reaction of HFP trimer with sodium 2,2,2-trifluoroethylate. The highly fluorinated enamine **5** resulted from the purification process of the crude material arising from the ECF fluorination of n-tributylamine. Treating the crude *F*-amine with alcoholic KOH, the major by-product, 1*H*-perfluorotributylamine, was converted to the well-characterized substituted amine **5** [6]. The unsaturated bis-trifluoromethyldioxolan **8** was prepared according to Ref. [7]. All fluoro-olefins to be fluorinated were checked spectroscopically by NMR and GC/MS, especially for the absence of isomers.

Fluorinations with N_2- or Ar-diluted elemental fluorine were performed with neat fluoro-olefins at room temperature in polyethylene bottles. In a standard example, about 20 ml of the unsaturated liquid was treated by bubbling the fluorine/argon mixture through it via a FEP capillary for 20–30 min. Optimum fluorination conditions for producing radicals were checked by ESR and IR spectroscopies. Extended fluorinations over 2 d were carried out in *F*-decalin as an inert solvent to study carbon bond splitting, CF_3 shifts as well as double-bond saturation. Reaction temperatures varied between 0–50 °C. Electrochemical fluorinations in AHF were undertaken as described elsewhere [8].

* Corresponding author.

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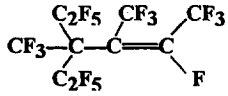
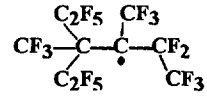
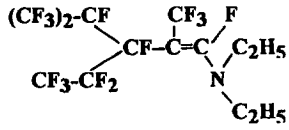
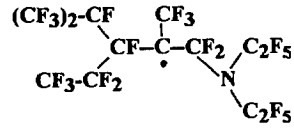
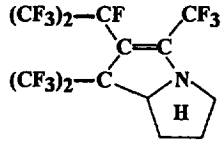
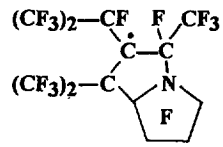
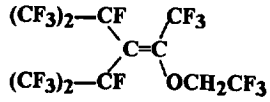
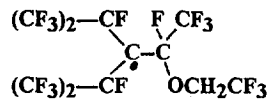
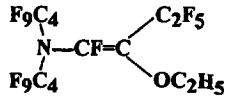
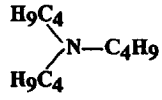
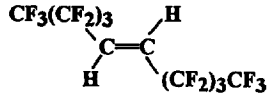
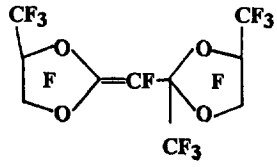
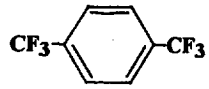
Table 1
ECF and elemental fluorinations of fluoroalkenes leading to radical generation

Reaction No.	Compound	Method	Radical
1		F_2	
2		F_2, ECF	
3		F_2, ECF	
4		F_2	
5		F_2	none
6		ECF	structure unknown
7		F_2	none
8		F_2	none
9		F_2	none

ESR measurements were recorded with a ZWG ERS 300 spectrometer at 9.5 GHz microwave frequency in the X-band using sealed 4 mm quartz tubes in a heatable equipment. Samples were diluted by perfluordecalin avoiding line broadening by spin exchange. ESR tomographic investigations were carried out with a 'modulated gradient and simultaneous field scan' (MOSS) technique with a spatial resolution of 15 μm. Samples were degassed, sometimes diluted and measured as liquids or solids (frozen in liquid N_2), aqueous solutions were measured in flat cuvettes at room temperature. Spectra were also recorded at elevated temperatures up to 160 °C to evaluate radical stabilities and resolution. Encapsulation of fluorocarbon radicals by emulsifiers, e.g. lecithin, to obtain aqueous biological compatible marker systems are described in Ref. [9].

3. Results and discussion

The compounds involved in this study to be fluorinated to radical species and the mode of fluorinations are listed in Table 1. Fluoroalkenes **1–4** were treated with argon-diluted fluorine. Because of the stepwise addition of atomic fluorine to the double bonds, radical centres are primarily formed. Consequently, radical annihilation can take place as a second fluorination step in the presence of excess fluorine but only at elevated temperature, forming the corresponding perfluoroalkane of **1** according to

$$CF_3C(C_2F_5)_2C(CF_3)=CFCF_3 \xrightarrow{+F^\cdot}$$

$$CF_3C(C_2F_5)_2\dot{C}(CF_3)CF_2CF_3 \xrightarrow{+F^\cdot}$$

$$CF_3C(C_2F_5)_2CF(CF_3)CF_2CF_3$$

At room temperature negligible amounts of the saturated compound are formed.

Depending on th substituents adjacent to the radical site, the spectra are split into multiplets. To evaluate the splitting pattern the rotational hindrance of the branched alkyl groups should be known, because the magnetic non-equivalence of the fluorine atoms caused by rotational hindrance makes basic changes in the hyperfine splitting. For compound **1**, the occurrence of rotational barriers can be ascertained by spatial modelling, as shown in Fig. 1. The major structural question of interest concerns the kind of hybridization at the paramagnetic carbon atom. For stereoactivity of the unpaired electron in a half-filled p_z orbital, a tetrahedral structure at the chiral sp^3 carbon is expected. On the other hand, a delocalized electron requires an sp^2 carbon with planarity. The latter is more convincing and will be discussed in a detailed analysis of the ESR spectrum of **1**, based on a space-filling model as well as on molecular calculations, to be given in a subsequent paper [10].

As mentioned above, the long-term stability can be explained as being a consequence of the strong branching of the molecule and the sterical shielding of the paramagnetic centre. Fig. 1 shows the geometric structure of compound **1** with the radical centre at the carbon atom at position 3.

At the same time, electron delocalization, i.e. electron withdrawal, into adjacent bonds occurs, as indicated by deviating chemical shifts and calculated charge densities [10]. Compound **1**, which is chemically the pentamer of tetrafluoroethylene, $C_{10}F_{20}$, is easily transformed into its radical. This gives a 10-line spectrum of 16.6 mT line width at room temperature. When heated to 140 °C, hyperfine splitting is observed (Fig. 2) because of the reduced spin–spin interaction and lowered inner viscosity. At this temperature a moderate decrease in spin density takes place, whereas at room

Fig. 1. Structural arrangement of the perfluoro-4-ethyl-3,4-dimethyl-3-hexyl radical.

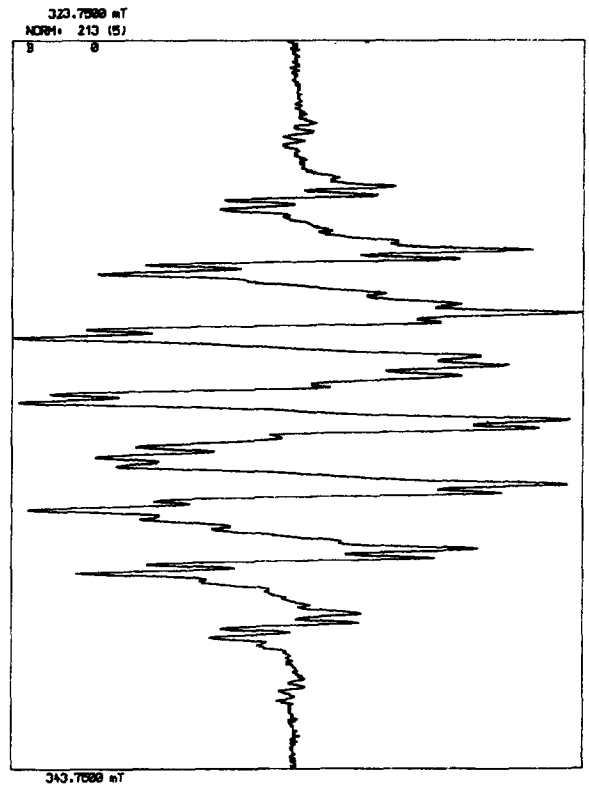


Fig. 2. ESR spectrum of the perfluoro-4-ethyl-3,4-dimethyl-3-hexyl radical at 140 °C; line width, 16.6 mT.

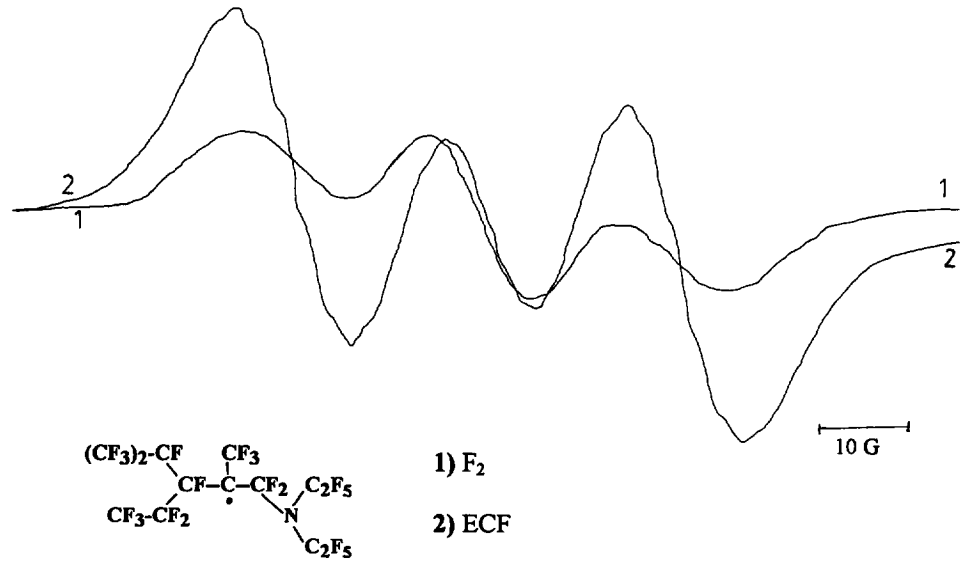


Fig. 3. ESR spectra: (1) elemental and (2) electrochemical fluorination of compound **2**.

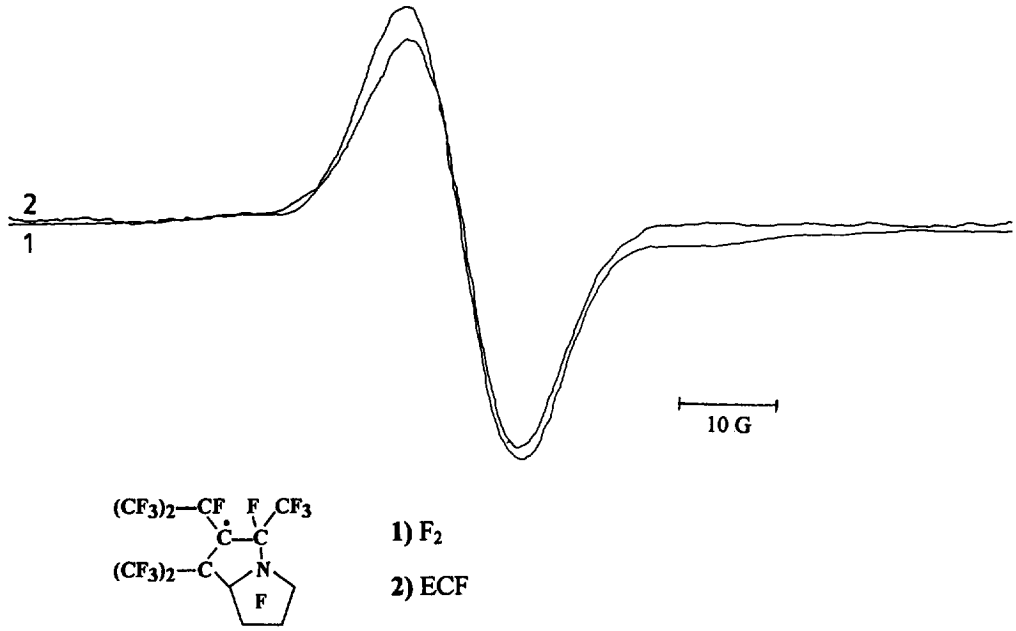


Fig. 4. ESR spectra: (1) elemental and (2) electrochemical fluorination of compound **3**.

temperature no changes have been observed over more than a year. Because the high-temperature decay is not accompanied by observable paramagnetic intermediates, the path of decomposition is a matter of speculation. Surprisingly, the radical is not oxidized in the presence of air. The simultaneous formation of peroxo radicals during the fluorination procedure has not been observed to date.

Compounds **2** and **3** were fluorinated by ECF in AHF as well as by standard procedures at Ni electrodes. The fluorination products were investigated by ESR spectroscopy and gave a broad absorption pattern with a triplet of 10 mT line width for **2** and a singlet of 4 mT for **3**, respectively. In the absence of a knowledge of the hyperfine splitting, the products from ECF and elemental fluorination appear to be identical with respect to their spectra (see Figs. 3 and 4). Because of this, we conclude that the two fluorination processes are similar. This generally means that in all cases radicals are formed by the action of atomic fluorine at the electron-deficient double bond. Consequently, ECF fluorinations in AHF must be considered to be radical processes with the formation of active fluorine.

Compound **4** is another example of a stable radical which gives a highly resolved ESR spectrum where the β-fluorine splits it into a doublet of 4.5 mT as shown by Scherer et al. [1]. Because of the proximity of the ether group, the β-fluorine atom is conformationally locked on the ESR time-

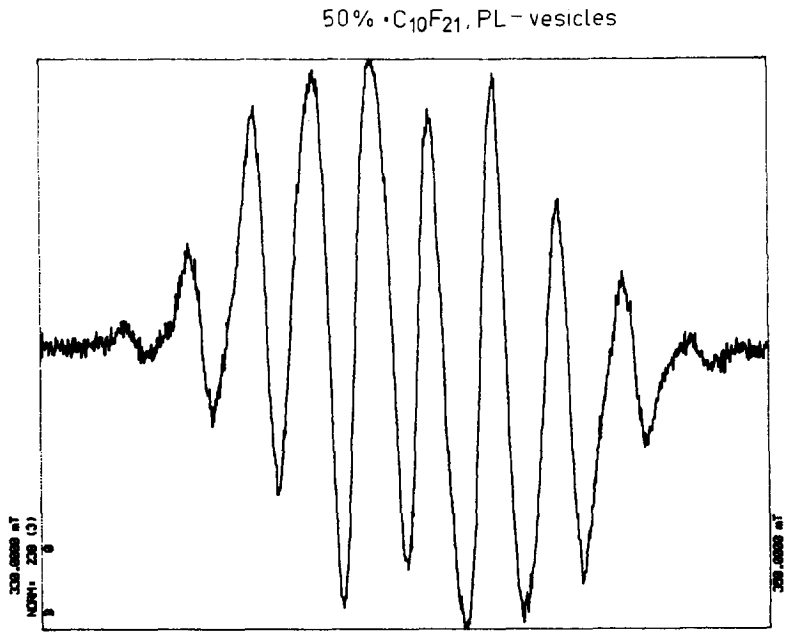


Fig. 5. ESR spectrum of the emulsified perfluoro-4-ethyl-3,4-dimethyl-3-hexyl radical in aqueous solution.

scale at room temperature. Heating leads to rearrangement to the known tris-*F*-isopropylmethyl radical. The reaction path is obviously in agreement with that described by Scherer et al., i.e. elimination of the alkoxy group and re-addition of a trifluoromethyl radical should take place.

Compounds **5, 7, 8** and **9** gave no detectable radical species when treated with fluorine. Obviously, the sterical peculiarities of these fully fluorinated olefins are not suited to support the formation and stabilization of radicals.

In the case of **6** and related non-fluorinated tertiary amines, especially those with bulky groups, small concentrations of radical species of unknown structure were observed during and after ECF fluorination. The samples were purged with argon and measured undiluted at room temperature. Their stabilities extended from only a few days up to a month. The observed radicals exhibit broad singlets and doublets, which might change. They were detected in both the crude electrofluorination products and in the highly fluorinated AHF phase. Because of the complex mixture of compounds, the radical centres cannot be assigned to individual molecular structures. It is thought that the radical could be located at a more crowded isotributylamine or at a substituted five-membered tertiary nitrogen cycle. Both types of structures are known to exist in the crude fluorination products of n-tributylamine.

Because of their unusual stability, stable radicals of the type discussed in this paper can be used as spin markers in organic media. Of greater interest, however, would be their use in aqueous solution, e.g. in biomedical systems. In principle, this can be attained by emulsifying the fluoro-organic liquid in water. Emulsification in water may be achieved by sonication or high-pressure homogenization with phospholipids or conventional surfactants as emulsifiers [9]; in all cases, stable emulsions were obtained. The radical itself was not affected by this procedure but remained unchanged as shown in Fig. 5. The fact that the radical is retained during the process of emulsification is somewhat surprising as it is well known that the high and very concentrated energy input involved in sonication can cause chemical alteration of the perfluorocarbons being emulsified.

An aqueous marker system prepared this way was used to study the penetration kinetics of phospholipid vesicles into the living skin tissue of mice [11]. Using the MOSS technique, images were produced depicting the radical concentrations in different skin planes.

4. Conclusions

The formation of stable radicals is not unusual in fluorinations in which fluorine radicals are involved. The occurrence of stable radicals in electrochemical fluorinations emphasizes the role of atomic fluorine in the ECF mechanism. Their high stability and very good detectability make these fluoro-organic radicals valuable markers.

Because their stability is comparable to that of perfluorocarbons in emulsification processes, fluoro-organic radicals can even be used as markers in biocompatible systems, thus opening access to a wide field of biological and medical applications.

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