

TECHNIQUES OF CHEMISTRY

VOLUME V, PART II

**TECHNIQUE OF
ELECTROORGANIC SYNTHESIS**

Edited by
NORMAN L. WEINBERG



TECHNIQUES OF CHEMISTRY

ARNOLD WEISSBERGER, *Editor*

VOLUME V, PART II

TECHNIQUE OF ELECTROORGANIC SYNTHESIS

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INTRODUCTION TO THE SERIES

Techniques of Chemistry is the successor to the Technique of Organic Chemistry Series and its companion—Technique of Inorganic Chemistry. Because many of the methods are employed in all branches of chemical science, the division into techniques for organic and inorganic chemistry has become increasingly artificial. Accordingly, the new series reflects the wider application of techniques, and the component volumes for the most part provide complete treatments of the methods covered. Volumes in which limited areas of application are discussed can easily be recognized by their titles.

Like its predecessors, the series is devoted to a comprehensive presentation of the respective techniques. The authors give the theoretical background for an understanding of the various methods and operations and describe the techniques and tools, their modifications, their merits and limitations, and their handling. It is hoped that the series will contribute to a better understanding and a more rational and effective application of the respective techniques.

Authors and editors hope that readers will find the volumes in this series useful and will communicate to them any criticisms and suggestions for improvements.

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ARNOLD WEISSBERGER

PREFACE

For too long the field of electroorganic synthesis has been considered "more of an art than a science." This attitude was appropriate until quite recently. However, the progress made in electroanalytical methods, especially in polarography and cyclic voltammetry of organic compounds, coupled with product isolation studies has given us new insight into the electrochemical reaction variables (potential, current density, adsorption, electrode material, etc.) and their interdependency. The result is that the organic chemist has at his disposal a highly useful synthetic tool, with great potentialities inherent in the technique for developing *electrode specific syntheses* including products that are not easily attainable by other methods.

For many years, the excellent chapter of Professor Sherlock Swann, Jr., in *Technique of Organic Chemistry* (Vol. II, 1956) has served as a primary source and incentive for those entering the field; but the technique of electroorganic synthesis has undergone much change since the appearance of that work. It has now become customary to carry out electrosyntheses under controlled potential conditions using three electrodes, the third one being a reference electrode. This contrasts with earlier synthetic studies in which constant current conditions were usually employed. This does not negate the value of the earlier literature. It is still important to know the products and which electrode material, added catalytic substances, pH, temperature, and so on were found necessary in a particular synthesis. Much can be learned from this older work which is directly applicable today. The new techniques using potentiostatic methods, however, are found superior mainly because they lead to fewer side products.

An approach for a particular synthesis that the organic chemist with a minimum of electrochemical background can easily follow involves, as a start, examination of the literature for suitable starting materials and conditions that fulfill the requirements of both the chemical and electrochemical reaction variables. This is followed by

1. setting up an electrochemical cell, usually with three compartments separating anode, cathode, and reference electrodes.
2. selection of a suitable controlled potential by determining current-potential curves on the background solution (solvent plus supporting

electrolyte) and with added substrate. The curves should be obtained on solutions with the concentrations of materials intended for use. Such curves are readily derived using a constant current power supply and a vacuum tube voltmeter, although a potentiostat is a great convenience (Chapter II). Knowledge of oxidation and reduction potentials (Chapter XII) can greatly aid in making a judicious choice of the operating electrode potential.

The electrolysis is carried out, products are isolated, and, if need be, the reaction variables are revised (these are often the electrode material and the solvent/supporting electrolyte) if necessary with repetition of steps 1 and 2.

The above is only one possible approach. Another approach involves the complementary use of electroanalytical methods to help sort out the possible reaction pathways and establish appropriate mechanisms (Chapters III and V).

The two parts of Volume V include the following:

1. An introduction to the field, valuable to the organic chemist in the laboratory as well as to the engineer considering scale-up (Chapter II).
2. A brief review of electrochemistry and the electroanalytical approach presenting some fundamental principles as well as an understanding of current problems (Chapters II, III, and V).
3. A critical review of the various electrochemical reactions of organic compounds, containing extensive tables of data (Chapters IV–XI).
4. Discussions of important electrosyntheses, including the scope, limitations, technical problems, comparisons with chemical methods, and mechanistic considerations.
5. Actual examples in recipe style.
6. Oxidation and reduction potential data in a form useful to the organic chemist (Chapter XII).

I sincerely thank the contributing authors for their painstaking efforts, conscientiousness of purpose, and patience. These works were envisioned by Dr. A. Weissberger to whom especial thanks are due. I am greatly indebted to Dr. Gerhard Popp of the Eastman Kodak Research Laboratories for his considerable help in reviewing the manuscripts. Thanks are due also to Professor Jack Stocker of Louisiana State University in New Orleans, Professor Albert J. Fry of Wesleyan University, and other reviewers acknowledged by the authors of this work. Their primary reward as well as mine will be to see the technique of electroorganic synthesis adopted into the arsenal of methods of organic chemists everywhere.

NORMAN L. WEINBERG

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Chapter VII

ELECTROCHEMICAL HALOGENATION OF ORGANIC COMPOUNDS

N. L. Weinberg

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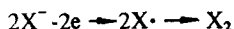
List of Symbols and Abbreviations:

The following symbols and abbreviations should be noted:

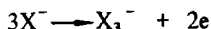
V	volt
A	ampere; mA, milliampere
i	current
CPE	controlled potential electrolysis
CD	current density
g	gram
Xg/Ygm	X grams product per Y grams starting material
F	Faraday (96,500 coulombs)
CE	current efficiency (%)
SCE	saturated calomel electrode

1 ELECTROCHEMICAL HALOGENATION

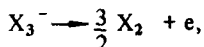
The oxidation potentials of halogen species in several media are listed in Table 7.1. The relative ease of oxidation is in the order $I^- > Br^- > Cl^- > F^-$, spanning almost the total available anodic range in which oxidation reactions of organic substrates have been studied. Thus in the discharge of halide ions according to the equations



or



and



it would be expected that anodic halogenation of a substrate S should proceed according to one or more of the following possibilities:

Route A: Discharge of S to a cationic intermediate followed by reaction with X^- .

Route B: Reaction of electrogenerated X_2 with S.

Route C: Reaction of electrogenerated X^\bullet with S.

Route D: Reaction of electrogenerated X_2 with solvent and S.

At present there are few clearly established examples of *Route A*, and it appears that starting substrate, solvent, or water in trace amounts competes effectively with X^- for the cationic species derived from the substrate. *Route B* involves the chemical reaction of electrogenerated halogen with substrate. This is generally a slow reaction for $X = I$ or Br compared to $X = Cl$ or F . Recent work on the bromination of aromatics [4] demonstrates that halogenation of anthracene occurs very poorly at the discharge potential of the halide. In contrast, halogenation does occur when the electrolysis is carried out at potentials more positive than the oxidation potential of the hydrocarbon, suggesting among other mechanisms, a reaction of cationic substrate with halide ion, or the discharge of a substrate — halogen charge transfer complex at the anode. *Route C* is possible with all of the halogens, but in the absence of high temperature and irradiation with light, is more important with $X = Cl$ and F . *Route D* is applicable to olefinic compounds in which the olefin reacts with electrogenerated halogen and a suitable solvent (see Part I, p. 368 for halofunctionalization of olefins). Thus in water, alcohols, or carboxylic acids, ROX [formed on discharge of X^- (R is H , alkyl or acyl)] may add to olefins. Alternatively the cyclic halonium ion species formed from olefin and X_2 may be attacked by solvent giving halofunctionalized products. Likewise amines and amides react with X_2 to give *N*-halo derivatives, which are known to add to certain olefins under various conditions. Acetonitrile is apparently iodinated during iodine oxidation to give *N*-iodoacetonitriliumion ($CH_3 - \overset{+}{C} = NI$), which serves as an iodinating agent for aromatics [5].

Experimental Parameters (General)

It is by now well recognized that such effects as adsorption and high rates of mass transfer of substrate to the electrode can lead to unexpected reaction paths that are not simply described by *Routes A → D*. Moreover, with judicious choice of parameters, what are often minor reaction paths can be maximized. Some general comments on important variables in halogenation reactions follow.

For halogenations in Cl^- , Br^- , or I^- electrolytes, there are no special requirements for anode materials other than that they be inert to electrochemical oxidation and the presence of electrogenerated halogen. Usually Pt and carbon in their various forms are suitable.

In contrast, fluorinations in liquid HF require nickel or carbon anodes for perfluorination to occur. As will be evident in the discussion on electrofluorination, the reaction on nickel appears to proceed on a high valent nickel fluoride surface, whereas the mode of reaction on carbon may be with adsorbed fluorine or fluorine atoms. Fluorinations on Pt have been carried out in CH_3CN , but the nature of the products are characteristic of reaction paths involving direct oxidation of the organic. Carbon anodes are consumed in molten inorganic fluoride media with production of short-chain perfluorocarbons.

Improved yields and fewer side products have been demonstrated with the use of nonaqueous media in halogenations using Cl^- , Br^- , and I^- solutions. Electrochemical perfluorinations require almost anhydrous HF, since the OF_2 produced from traces of water is a powerful oxidizing agent and causes explosions when admixed with organic materials.

Table 7.1 Oxidation Potentials of Halogen Species

Halogen Couple	$E_{1/4}$ At Pt (V vs SCE) ^a			
	CH_3CN	DMF	DMSO	E_0 (V vs NHE) ^c
I^-/I_2 (or I_3^-)	0.20	0.50	0.45	0.54
I_3^-/I_2	0.55	0.62	0.60	—
$\text{I}_2/\text{I}_2^{\cdot+}$ (?)	2.2 ^b	—	—	—
Br^-/Br_2	0.70	0.65	0.60	1.09
$\text{Br}_3^-/\text{Br}_2$	0.95	0.85	0.85	—
Cl^-/Cl_2	1.15	1.02	1.00	1.36
F^-/F_2	—	—	—	2.87

^aSee Ref. 1.

^bSee Ref. 2.

^cSee Ref. 3.

Generally, radical halogenation reactions of lower specificity predominate with higher temperatures; but in some cases higher temperatures may be required to effect any reaction. For example, *n*-dodecane, which does not react

with Cl_2 to any appreciable extent at room temperature, gives a mixture of primary monochlorides, secondary monochlorides, and dichlorides in 44% CE at 93°C [6].

Use of high current densities will require the use of higher potentials, resulting in electrooxidation of the halogenated product. This is especially true for iodinated and brominated products, which are readily electrooxidized [2]. Chlorinated and fluorinated products are relatively inert to further oxidation.

One important effect of high current density is to increase the concentration of radicals ($\text{X}\cdot$) at the anode surface. Thus radical abstraction of hydrogen by halogen may be expected to become important. The effects of current density and potential are discussed in greater detail under the appropriate halogenation reaction.

Partial fluorination generally occurs most successfully with increasing concentration of substrate. In contrast, the formation of bromoform and iodoform from acetone or ethyl alcohol appears to proceed best at high concentration of substrate.

Porous electrodes have been used for introducing a high concentration of a gaseous substrate through the anode. Nagase [7] has reviewed the use of this method for fluorination of a wide range of gaseous or low boiling substances.

Electrochemical Fluorination

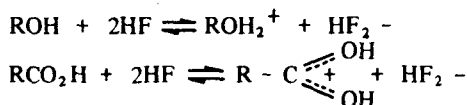
Credit for the first electrochemical fluorination has always been given by reviewers to Lebeau and Damiens [8], who isolated CF_4 during electrolysis of molten beryllium fluoride at a carbon anode. Actually Lyons and Broadwell [9] produced CF_4 more than two decades earlier by electrolyzing a melt (1000°C) of sodium and potassium fluorides at a graphite anode surrounded by carbonaceous material.

In contrast, the Simons method, discovered in 1941, may be described as the low-temperature electrolysis at a Ni anode of an organic compound, dissolved or suspended in liquid HF, to give a perfluorinated product. A large number of compounds have been subjected to the Simons procedure [7, 10-17], but results obtained for the same reaction by different laboratories show that reproducibility is apparently difficult to achieve.

Physical and Chemical Properties of Liquid HF

Hydrogen fluoride is an ideal solvent for electrochemical studies with a convenient boiling point (19.5°C), high dielectric constant, low viscosity, and powerful solubilizing ability for a wide range of organic as well as inorganic compounds. It has the disadvantage of dissolving glass. Fortunately, however, there are many materials available now that are useful, such as inert plastics (Teflon^R, polyethylene, polypropylene, Vitron^R, Kel-F^R, and FEPR^R); [18]; there is also Pt, which is not attacked, and Cu, Ni, Mg, and Al, which form protective fluoride coatings.

Many organic compounds dissolve in liquid HF to give conducting solutions. Weak bases such as ethanol, acetone, and acetic acid behave as strong electrolytes with conductances similar to that of fluorides [19]. Spectroscopic and other studies have established that these compounds are protonated in HF [20]:



Aromatic hydrocarbons behave similarly [20a]:



The least soluble materials in HF are saturated hydrocarbons and especially, perfluorinated hydrocarbons.

Liquid HF can cause partial fluorination to some extent with several classes of organic compounds. Addition occurs to olefins and acetylenes, while carboxylic acids, anhydrides, and chlorides are converted to the corresponding carboxylic acid fluorides.

Experimental Technique

The electrochemical variables for electrofluorination of organic compounds have traditionally been expressed as cell voltage (5-7 V) and current density (0.0008 - 0.02 A/cm²). Only a few electrochemical studies, confined to the investigation of inorganic fluorination reactions, have been reported using reference electrodes. This unfortunate situation exists in spite of the fact that reference electrodes for liquid HF have been developed. These include the Hg/Hg₂F₂ electrode [21, 22] and the Cu/CuF₂ couple [23]. Not only could a clearer understanding of the reaction mechanism be possible, but control of the electrode potential could possibly result in higher yields of desired product and reproducibility of results.

The most practical anode material [24, 25] has been Ni or a Ni alloy such as Monel (66% Ni), although some studies have employed carbon or platinum under special conditions. Other anodes and anodes of metals of which the higher fluorides are used as chemical fluorinating agents were found unsuitable because of corrosion, passivation, or little or no fluorination product formed. Recently, the use of a porous carbon anode in a solution of composition KF.2HF at about 100°C has been shown by Fox et al. [25a] to give excellent results in partial fluorination reactions. An essential feature of this novel process is that the insoluble feed is kept confined to the pores of the porous carbon anode and is not permitted to break out into the bulk of the solution.

Further characteristics of electrofluorination include the following: Use of a

rotating anode or pumping the HF solution through a porous anode (especially for gaseous or insoluble substrates) raises the yield of product substantially; since most perfluorinated compounds are inert to electrochemical reductions, diaphragms or separators are not required; cathode materials of Ni, Fe, Cu, or Pt are suitable, but those of Al, Zn, and Pb have a deleterious effect on the reaction; electrolysis temperatures near 0°C are most often used, but higher temperatures may be practical; conductivity additives such as NaF or KF are needed with nonconducting substrate-HF solutions; with conducting substrate-HF solutions the end of the electrolysis is signalled when the current has dropped to a low value, since perfluorinated compounds are usually nonconducting; often a preelectrolysis of the HF solution without the substrate is carried out to remove small amounts of water present in the solvent (Note. The oxygen difluoride that is formed is a powerful oxidizing agent and can be explosive when concentrated with organics).

A typical industrial fluorination cell is described in Chapter II, p. 135.

Experimental Examples

Dr. Shunji Nagase (Government Industrial Research Institute, Nagoya, Japan) has kindly provided the following examples which typify many aspects of the technique of electrofluorination.

PARTIAL FLUORINATIONS OF METHANE (PREPARATION OF FLUORINATED METHANES) [26]

Apparatus. The apparatus consists essentially of an electrolytic fluorination cell, hydrogen fluoride absorber, oxygen difluoride absorber, and a series of cold traps as shown in Fig. 7.1. The electrolytic cell is a cylindrical Monel vessel, 10 cm in diameter and 21 cm long, provided with a copper condenser at the top to condense vaporizing hydrogen fluoride. The electrodes consist of eight and nine pieces of nickel plates (0.5 mm in thickness) as anodes and cathodes, fastened together alternately, suspended from the top, and insulated from each other by poly(tetrafluoroethylene) pieces. The distance between the plates is 1.7 mm and the effective surface area of the anodes and cathodes is 9.2 dm².

A copper spiral tubing is provided inside the cell to maintain the optimum temperature by circulation of ice water during the reaction. The bubbler that is placed at the bottom of the cell consists of a 6 × 15-mm polyethylene tube, with an internal diameter of 4 mm whose tip is enlarged to 8 mm in diameter and capped with a woven fabric made of poly(tetrafluoroethylene).

The hydrogen fluoride absorber is an iron tube containing a bed of sodium fluoride pellets that absorb uncondensed hydrogen fluoride escaping from the reflux condenser. As an oxygen difluoride absorber, gas-washing bottles containing an aqueous solution of sodium sulfite with a small amount of potassium iodide are used. (Anhydrous hydrogen fluoride has a strong affinity for water, and commercial hydrogen fluoride contains a trace of dissolved water

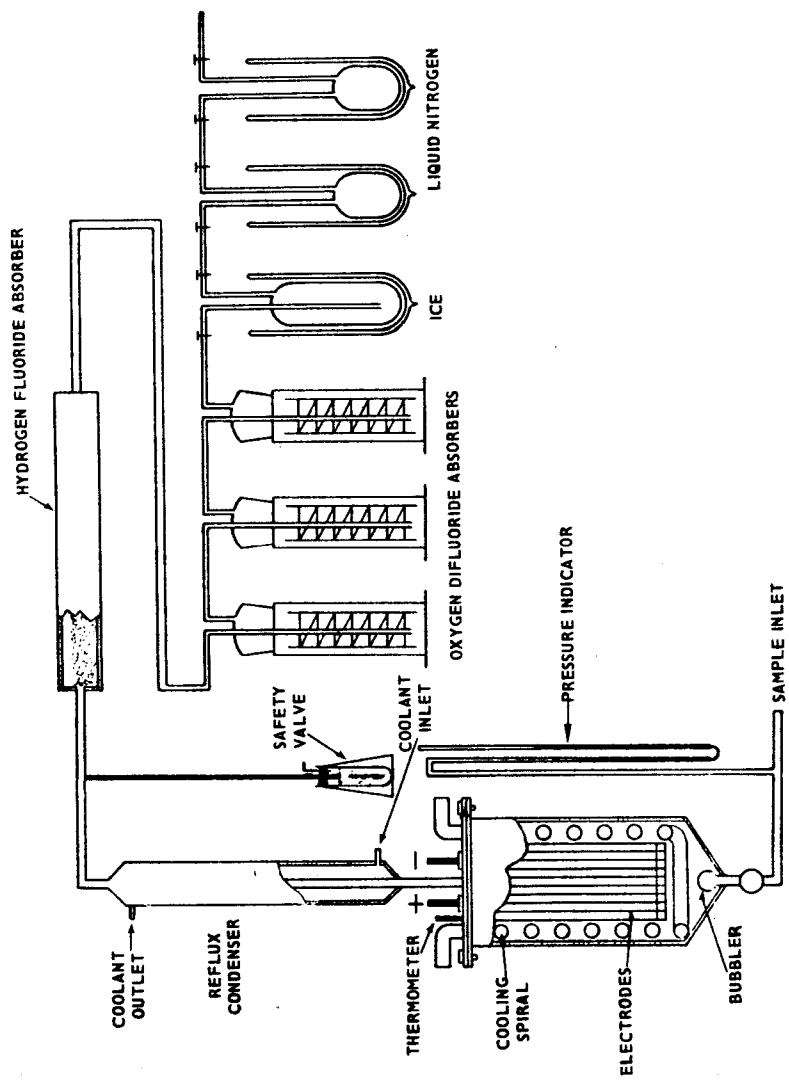


Fig. 7.1 Electrofluorination apparatus.

that can be removed by passing a current through it. Therefore, electrochemical fluorination is often accompanied by the formation of oxygen difluoride [27], especially in preliminary electrolysis.) Mercury in the safety valve and in the pressure indicator is covered by fluorocarbon oil.

Procedure. Anhydrous hydrogen fluoride (1 liter) is placed in the cell and, in order to remove traces of impurities (mainly water), electrolysis is carried out in a nitrogen atmosphere, prior to the introduction of methane, with an anodic current density of 2.7 A/dm^2 and at $5\text{--}6^\circ\text{C}$, until the cell voltage rises to 6.0 V . Then 10 g of sodium fluoride (conductivity additive) is added, and metered methane is introduced from the bottom of the cell into hydrogen fluoride maintained at $5\text{--}6^\circ\text{C}$, through the bubbler at a flow rate of 65 ml/min . Electrolysis is conducted at an anodic current density of 2.2 A/dm^2 . When the cell voltage becomes almost steady at $6\text{--}6.5 \text{ V}$, the traps are placed in ice and liquid nitrogen, respectively, and electrolysis is carried out for 71 A hr .

Fluorinated gas evolved from the cell passes through a reflux condenser kept at -20°C and over a bed of sodium fluoride pellets, then bubbles through an aqueous solution of sodium sulfite, and finally condenses in cold traps. The product obtained is rectified in a low-temperature rectification unit. Each fraction is further analyzed by gas chromatography using an activated charcoal column, 2 m long, maintained at 70°C (carrier gas is helium):

Rectification of Fluorinated Methane

<i>Fraction No.</i>	<i>Boiling Point ($^\circ\text{C}$)</i>	<i>Wt. (g)</i>	<i>Component</i>
1	$-162 \text{ to } -159$	5.6	CH_4
2	$-128 \text{ to } -126$	6.7	CF_4
3	$-80 \text{ to } -76$	6.1	CH_3F , CHF_3
4	-70 to hold up	2.0	CH_3F , CHF_3 , CH_2F_2

Product composition (mole %): CF_4 , 29.0%; CHF_3 , 12.3%; CH_2F_2 , 12.7%; CH_3F , 46.0%

Conversion: 43%

Total current efficiency: 44%

FLUORINATION OF ETHYL ACETATE (PREPARATION OF SODIUM TRIFLUOROACETATE) [28]

Apparatus. The apparatus consists of an electrolytic cell, hydrogen fluoride absorber, and fluorinated product trap. The electrolytic cell (made of a nickel vessel), which is not equipped with the bubbler, and the hydrogen fluoride absorber are virtually the same as those described above. The product trap consists of a pair of polyethylene bottles containing 200 and 500 ml of water.

Procedure. Ethyl acetate (34.5 g) is dissolved in anhydrous hydrogen fluoride (1 liter) that had been purified by electrolysis, then electrolysis of the solution is carried out with an anodic current density of 3.3 A/dm^2 at an average of 4.8 V at $4-6^\circ\text{C}$ for 221 A hr. At the end, the voltage rises up to 5.3 V.

The outgoing gases, such as trifluoroacetyl fluoride, fluorocarbons, oxygen difluoride, hydrogen, and so on, from the cell are passed through the reflux condenser kept at -20°C into the hydrogen fluoride absorber, and are bubbled through the water in the product trap where trifluoroacetyl fluoride is converted into trifluoroacetic acid. In this system, gases that are inert to water should escape.

The aqueous solution of trifluoroacetic acid in the absorber is neutralized with sodium carbonate, and filtered. The filtrate is evaporated to dryness. Extraction of the resulting crude sodium trifluoroacetate with absolute ethanol followed by evaporation of the solvent affords sodium trifluoroacetate (54.2 g), as follows:

Yield, 51.6%; current efficiency, 40.5%.

General Scope and Limitations

Unless special provision in the electrochemical method is made, all the hydrogens of the organic substrate are replaced by fluorine. Partial fluorination may be achieved, however, by using a high concentration of the substrate [29, 30] and low current density, or in the case of gaseous substrates, bubbling these diluted with inert gas through the cell. By adjusting the feed rate, some optimization of yield toward desired products is accomplished. Thus for methane, Nagase and co-workers [26] have found a marked effect of feed rate on the yields of various partially fluorinated methanes from methane (Table 7.2).

Table 7.2 Partial Fluorination of Methane

Feed Rate (ml/min)	% Product Composition				Total % Yield	Total % Current Efficiency
	CF ₄	CHF ₃	CH ₂ F ₂	CH ₃ F		
42	34	20	18	28	48	38
64	29	12	13	46	43	44
104	24	11	18	57	32	48

For nongaseous substrates, cell designs providing for short contact time at the electrode should likewise afford enhanced yields of partially fluorinated products.

Many compounds are fluorinated with preservation of functional groups and the original carbon skeleton. If cleavage does occur between a carbon and a functional group (C-halogen, C-O, C-N, C-S, C-Si, etc.) the parent fluorocarbon is often the resultant product.