



Fluorine in Organic Chemistry

R. D. CHAMBERS, Ph.D., D.Sc.

READER IN ORGANIC CHEMISTRY
UNIVERSITY OF DURHAM, ENGLAND

A WILEY-INTERSCIENCE PUBLICATION

JOHN WILEY & SONS

New York · London · Sydney · Toronto

Copyright © 1973, by John Wiley & Sons, Inc.

All rights reserved. Published simultaneously in Canada.

No part of this book may be reproduced by any means, nor transmitted, nor translated into a machine language without the written permission of the publisher.

Library of Congress Cataloging in Publication Data:

Chambers, Richard D.

Fluorine in organic chemistry.

(Interscience monographs on organic chemistry)

"A Wiley-Interscience publication."

Includes bibliographical references.

I. Organofluorine compounds. I. Title.

QD412.F1C47 547'.02 73-7824

ISBN 0-471-14330-8

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

Fluorine in Organic Chemistry

INTERSCIENCE MONOGRAPHS ON ORGANIC CHEMISTRY

EDITOR: George A. Olah

**DEPARTMENT OF CHEMISTRY
CASE-WESTERN RESERVE UNIVERSITY
CLEVELAND, OHIO**

Sulfonation and Related Reactions

BY EVERETT E. GILBERT

Peptide Synthesis

BY MIKLOS BODANSZKY AND MIGUEL A. ONDETTI

1,2-Cycloaddition Reactions: The Formation of Three- and Four-Membered Heterocycles

BY LINDA L. MULLER AND JAN HAMER

Mechanistic Aspects in Aromatic Sulfonation and Desulfonation

BY HANS CERFONTAIN

Friedel—Crafts Chemistry

BY GEORGE A. OLAH

Fluorine in Organic Chemistry

BY R. D. CHAMBERS

TO

Anne, Mark, and Louise

Editor's Introduction

The chemical literature in recent years increasingly emphasized multi-author monographs covering broader topics or review articles as part of the numerous "Advances" or "Progress" series. Both fill important needs and became integral parts of our libraries as valuable reference sources. By their nature and price they, however, rarely can reach the desks of individual chemists for their personal use. They also reflect the fact that the evergrowing chemical literature makes it increasingly difficult for individual authors to cover larger fields in a comprehensive and critical way.

To contribute a chapter or to write a review article frequently involves an effort comparable to that of writing a monograph on the topic. There is a genuine and growing need for authentic monographs written by experts actively engaged in research in their respective fields of specialization. These can provide not only a review of the topic, but more importantly, they can critically evaluate the field, point out the major and most important advances achieved, and also possible new avenues of approaches where further future research is most needed. These smaller monographs using improved technical methods can be produced faster and cheaper than multi-author collective volumes, where the "slowest" author or editor inevitably determines the speed of publication. Individual monographs also give full recognition to the author, which is not always possible, if for no other than technical reasons, in edited volumes.

The foregoing were the main reasons which caused the editor and the publishers to initiate a series of monographs in Organic Chemistry. Similar monographs are being published in the field of Inorganic and Physical Chemistry. The Organic Chemistry Section of the Interscience Monographs on Chemistry will be accessible to the average chemist for his own use at reasonable prices and will provide titles of current interest in a wide scope. It is hoped that the high standard and timeliness of these volumes aimed at by the authors, the editors, and the publisher will make them a useful addition to the chemical literature.

GEORGE A. OLAH

Preface

This book grew out of a course of lectures given to graduate students while the author was a visiting lecturer at Case-Western Reserve University, Cleveland, Ohio, and I welcome the opportunity of thanking Professor George Olah for the hospitality of his department. An attempt has been made here to describe organic fluorine chemistry with a particular stress on mechanism and the relevance to organic chemistry at large. No attempt has been made to present a comprehensive coverage of the vast literature now available on the subject. Inevitably, this selective approach has left out material that others would like to see covered, and I apologise in advance to authors whose work is not included; also, I am afraid that I have probably done less than justice to the fine contributions of our friends in Russia because of the difficulties of translation. The cut off point for literature is essentially the end of 1971, although some of the more recent references are included.

I would like to thank my colleague, Professor W. K. R. Musgrave, who originally introduced me to this subject, for his encouragement and for his helpful comments on the manuscript. I am also grateful to Dr. Hugh MacBride and Dr. David Spring for reading the manuscript and for their numerous helpful comments. My thanks also go to Mrs. E. Duddy and Mrs. E. McGauley, for typing the manuscript, Mrs. R. MacBride, for illustrations, and last, but not least, to my wife Anne and our children Mark and Louise, for their continued understanding.

DICK CHAMBERS

Durham, England
June 1973

Contents

1. General Discussion of Organic Fluorine Chemistry	1
I. General Introduction	1
A. Properties	1
B. Reaction Mechanisms	2
C. Industrial Applications	3
II. Electronic Effects in Fluorocarbon Systems	4
III. Nomenclature	8
A. Two Systems of Nomenclature	8
B. Haloalkanes	10
IV. Historical Development	10
References	11
2. Preparation of Highly Fluorinated Compounds	14
I. Source of Fluorine	14
II. Fluorination with Metal Fluorides	15
A. Swarts Reaction and Related Processes (Halogen Exchange)	15
B. Alkali-Metal Fluorides	20
C. High Valency Metal Fluorides	24
III. Electrochemical Fluorination	26
IV. Fluorination with Elemental Fluorine	29
A. Fluorine Generation	29
B. Reactions	29
C. Control of Fluorination	30
D. Graphite Fluorides	32
E. Fluorination of Compounds Containing Functional Groups	32
V. Halogen Fluorides	33
References	34

3. Partial or Selective Fluorination	38
I. Displacement of a Single Atom or Group Using Metal Fluorides	38
A. Silver (I) and Mercury (I) Fluorides	39
B. Silver (II) and Mercury (II) Fluorides	39
C. Alkali-Metal Fluorides	40
II. Replacement of Hydrogen by Fluorine	41
A. Elemental Fluorine	41
B. Perchloryl Fluoride	41
C. Photofluorination	45
III. Replacement of Hydroxyl by Fluorine	45
IV. Miscellaneous	46
A. Alkyl Fluorides	46
B. Cleavage of Epoxides	47
V. Fluorination of Carbonyl Compounds and Others	48
A. Sulphur Tetrafluoride	48
B. Molybdenum Hexafluoride	52
C. Halogen Fluorides	52
VI. Additions to Olefins and Acetylenes	53
A. Addition of HF	53
B. Direct Addition of F ₂	54
C. Indirect Addition of F ₂	55
D. Addition of the Elements of BrF and IF	57
E. Addition of Fluoroxy Compounds (Hypofluorites)	58
References	59
4. The Influence of Fluorine of Fluorocarbon Groups on Some Reaction Centres	64
I. Introduction	64
II. Electronic Effects of Polyfluoroalkyl Groups	65
A. Saturated Systems	65
B. Unsaturated Systems	67
III. Strengths of Unsaturated Fluoro Acids and Fluoro Bases	71
IV. Fluorocarbonium Ions	73
A. Effect of Fluorine as a Substituent in the Ring on Electrophilic Aromatic Substitution	73

B.	Electrophilic Additions to Fluoro Olefins	76
C.	Relatively Stable Fluorocarbonium Ions	78
D.	Fluoromethyl Cations	80
E.	Effect of Fluorine Atoms Not Directly Conjugated with the Carbonium Ion Centre	81
V.	Fluorocarbanions	84
A.	Fluorine Atoms Attached to the Carbanion Centre	85
B.	Fluorine Atoms and Fluoroalkyl Groups Adjacent to the Carbanion Centre	89
C.	Acidities of Fluorobenzenes and Derivatives	91
D.	Acidities of Fluoro Olefins	92
	References	95
5.	Nucleophilic Displacement of Halogen from Fluorocarbon Systems	97
I.	Substituent Effects of Fluorine or Fluorocarbon Groups on the S_N2 Process	97
II.	Fluoride Ion as a Leaving Group	99
A.	S_N1 and S_N2 Processes	99
B.	Addition-Elimination Mechanism	104
	References	108
6.	Elimination Reactions	109
I.	β Elimination of Hydrogen Halides	109
A.	Effect of the Leaving Halogen	109
B.	Substituent Effects	110
C.	Orientation of Olefins Produced	112
D.	Conformational Effects	113
E.	Elimination from Cyclic Systems	114
II.	β Elimination of Metal Fluorides	117
III.	α Eliminations, Generation, and Reactivity of Fluro- carbenes and Polyfluoroalkylcarbenes	119
A.	Fluorocarbenes	120
B.	Polyfluoroalkylcarbenes	129
C.	Structure and Reactivity of Fluorocarbenes and Polyfluoroalkylcarbenes	131
	References	134

7. Polyfluoroalkanes, Polyfluoroalkenes, Polyfluoroalkynes, and Derivatives	138
I. Perfluoroalkanes and Perfluorocycloalkanes	138
A. Bonding in Fluoromethanes	138
B. Carbon-Carbon Bond Strengths	139
C. Physical Properties	140
D. Chemical Reactions	141
II. Perfluoroalkenes and Perfluorocycloalkenes	142
A. Stability	142
B. Synthesis	144
C. Nucleophilic Attack	148
D. Electrophilic Attack	170
E. Free-Radical Additions	173
F. Cycloadditions	179
III. Fluoroacetylenes and Fluoroalkylacetylenes	189
A. Fluoroacetylenes	189
B. Perfluoroalkylacetylenes	191
C. Reactions	192
References	199
8. Functional Compounds Containing Oxygen, Sulphur, or Nitrogen and Their Derivatives	209
I. Oxygen Derivatives	209
A. Carboxylic Acids	209
B. Ketones	216
C. Perfluoroalcohols	225
D. Fluoroxy Compounds	228
E. Perfluoroepoxides	229
F. Peroxides	232
II. Sulphur Derivatives	233
A. Perfluoroalkanesulphonic Acids	233
B. Sulphides and Polysulphides	235
C. Thiocarbonyl Compounds	239
III. Nitrogen Derivatives	241
A. Amines	241
B. N-O Compounds	243
C. Aza Alkenes	245
D. Azo Compounds	248
E. Diazo Compounds and Diazirines	249
References	252

9. Polyfluoroaromatic Compounds	261
I. Synthesis	261
A. General Considerations	261
B. Saturation Rearomatisation	262
C. Substitution Processes	265
II. Properties and Reactions	274
A. General	274
B. Nucleophilic Aromatic Substitution	275
C. Reactions with Electrophilic Reagents	308
D. Free-Radical Attack	313
E. Reactive Intermediates	317
References	334
10. Organometallic Compounds	344
I. General Methods of Synthesis	345
A. From Iodides, Bromides, and Hydro Compounds	345
B. From Unsaturated Fluorocarbons	346
II. Lithium and Magnesium	347
A. From Saturated Compounds	347
B. From Olefins	351
C. From Trifluoropropyne	352
D. From Polyfluoroaromatic Compounds	353
III. Zinc, Cadmium, and Mercury	353
A. Zinc	353
B. Cadmium	354
C. Mercury	355
IV. Boron, Aluminum, Thallium	359
A. Boron	359
B. Aluminum	363
C. Thallium	364
V. Silicon, Germanium, Tin, and Lead	365
A. Silicon	365
B. Germanium, Tin, and Lead	367
VI. Transition Metals	370
A. Copper, Silver, Gold	371
B. Other Metals	373
References	378
Index	385

1. General Discussion of Organic Fluorine Chemistry

I. GENERAL INTRODUCTION

Fluorine is unique in that it is possible to replace hydrogen by fluorine in a wide range of hydrocarbon systems without gross distortion of the geometry of the system. With minor exceptions, fluorocarbon compounds do not occur in nature and so, potentially, we have a complete organic chemistry available that is entirely synthetic. Consequently the study of the chemistry of fluorocarbon systems has now become an important area of research and the subject constitutes a major branch of organic chemistry. Nevertheless, this situation is not yet reflected in current general textbooks and the reason for this can easily be attributed to the very rapid growth of the subject. It is hoped that this book will help by presenting an outline of fluorine chemistry on a broadly mechanistic basis. The author acknowledges the reviews published in various books or journals, either referred to here [1-7] or in the following text, and other books on the subject or aspects of it [8-17] to which this book is intended to be complementary. In 1971, the *Journal of Fluorine Chemistry* was established and also a Specialist Periodical Report of the Chemical Society, *Fluorocarbon and Related Chemistry*, was begun.

A. Properties

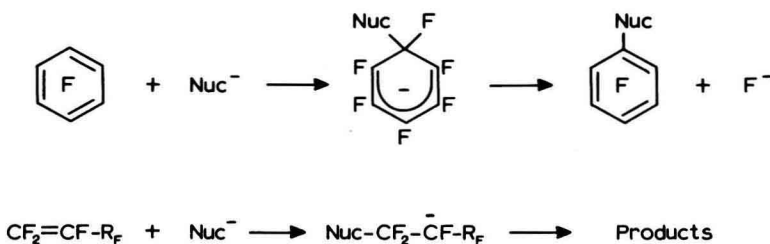
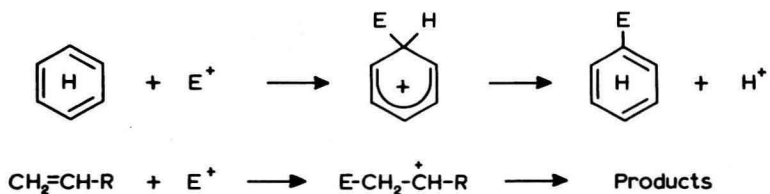
Contrary to what appears to be quite common belief, fluorocarbon systems, in general, present no peculiar handling difficulties and the familiar and powerful

techniques of isolation, purification, and identification are applicable in ways similar to those for corresponding hydrocarbon systems. In fact fluorocarbons themselves are characterised by high thermal stability and, indeed, elemental fluorine is so very reactive because it forms strong bonds with other elements, including carbon. Volatilities of hydrocarbons and corresponding fluorocarbons are surprisingly similar, despite the increased molecular weight of the latter, and indicate a general feature that intermolecular bonding forces are reduced in the fluorocarbon systems. A final, and by no means least important, similarity between hydrocarbon and fluorocarbon chemistry is that, like hydrogen-1, fluorine-19 has a nuclear spin quantum number of $\frac{1}{2}$ and so the nuclear magnetic resonance experiment can be applied in an analogous way. In fact, the only tool that is not easily available for fluorine is the observation of fluorine-isotope effects, because no isotope of fluorine with a useful lifetime exists (the longest lived isotope is ^{18}F , with a half-life of 109 minutes).

B. Reaction Mechanisms

It may be asked at this point what the benefits of a study of this chemistry are. First, the difference between hydrogen and the most electronegative element, fluorine, creates in the fluorocarbon system entirely different electronic environments for functional groups. Consequently, new compounds become available with reactions and properties quite different from their hydrocarbon analogues and this automatically poses a strenuous test on our theories of reaction processes and factors affecting reactivity. Although steric effects must be important, the differences in properties between hydrocarbon and fluorocarbon systems are not dominated by gross differences in stereochemistry.

The sometimes complementary nature of the chemistry of hydrocarbon and fluorocarbon systems can be illustrated by reference to olefins and aromatic compounds. Whereas the chemistry of hydrocarbon aromatic compounds and olefins most frequently involves attack by electrophiles leading to carbonium-ion-type transition states, fluorocarbon aromatic compounds and olefins more frequently undergo nucleophilic attack leading to carbanionic transition states. Therefore, while the hydrocarbon derivatives are the natural parent compounds for the study of the mechanisms of processes involving electrophilic attack, it can be argued that the fluorocarbon derivatives are the more appropriate parent compounds on which to base a study of nucleophilic attack in these systems.



C. Industrial Applications

Another important aspect of this chemistry is the number of industrial applications and potential applications of the new materials that are being discovered [1]. The most obvious area of application is in the field of thermal and chemically stable materials; for example, microbiological oxidation of perfluoroalkanes does not appear to occur. Freons,* the most important group of fluorocarbon products, are produced on a massive and ever increasing scale, being used now, in addition to their original application as refrigerants, as inert aerosol propellants, and the like. Polytetrafluoroethylene, which is rapidly acquiring an astonishingly wide range of applications, and Fluothane,† said to be the best general anaesthetic ever available, also spring to mind as spectacular successes. However, there is a wide range of fluorocarbon or partly fluorinated materials in use, some of which are referred to in Table 1.1.

*Trade name of E. I. du Pont de Nemours Inc., U.S.A.; other companies have a variety of appropriately similar names for this group of compounds.

†Trade name of Imperial Chemical Industries Ltd., U.K.

Table 1.1. Some Industrial Applications of Fluorocarbon Materials [18,19]

Product	Applications
Polyfluoroalkanes and cycloalkanes, e.g., CF_2Cl_2 ; $\text{CF}_2\text{Cl}\cdot\text{CFCl}_2$	Refrigerants; aerosol propellants; solvents; blowing agent for foam plastics
Bromofluoroalkanes, e.g., CF_3Br	Fire extinguishers
CF_3CHClBr (Fluothane) (I.C.I.)	General anaesthetic
Metal salts of various perfluoroalkane carboxylic and sulphonic acids, R_FCOOM , $\text{R}_F\text{SO}_3\text{M}$	Surface-active agents
Monofluoroacetamide	Systemic insecticide and rat poison
Polytetrafluoroethylene $(\text{CF}_2)_n$	High thermal and chemical stability and anti-stick properties; good electrical insulator
Polychlorotrifluoroethylene $(\text{CF}_2-\text{CFCl})_n$ (Kel F) (3M)	Good thermal and chemical stability lubricants
Copolymer of $\text{CH}_2=\text{CF}_2$ and $\text{CF}_3\cdot\text{CF}=\text{CF}_2$. (Viton A) (Du Pont) $[\text{CH}_2-\text{CF}_2-\text{CF}_2-\text{CF}(\text{CF}_3)]_n$	High chemical and thermal stability elastomer
Methyl-3,3,3-trifluoropropyl silicone. $[(\text{CF}_3\text{CH}_2\text{CH}_2)(\text{CH}_3)\text{SiO}]_n$	Elastomer with high chemical and thermal stability
Polyvinylfluoride $(\text{CH}_2-\text{CHF})_n$	Coating material, very weather resistant
Telomers of tetrafluoroethylene $\text{X}(\text{CF}_2\text{CF}_2)_n\text{Y}$	Metal-working lubricants and gyro fluids
Alcohol derivatives containing a terminal fluoroalkyl group	Grease-proofing agents for paper; stain repellants for textiles
Fluoro steroids	Pharmaceuticals
Dyes containing CF_3 groups	Good light fastness

II. ELECTRONIC EFFECTS IN FLUOROCARBON SYSTEMS

The electronic properties and size of fluorine relative to hydrogen and chlorine are set out in Table 1.2 and at this point it is worthwhile to examine some of the possible consequences of these differences on the chemistry of fluorocarbon systems. In this way it can be emphasised, at the outset, how far-reaching these effects will be and, at the same time, set the scene for a rational approach to the chemistry.

First, the large ionisation energy of fluorine implies that species involving electron deficient fluorine might be less common than those involving hydrogen or