
FLUORINE IN ORGANIC CHEMISTRY

Richard D. Chambers



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Fluorine in Organic Chemistry

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Fluorine in Organic Chemistry

To
my wife Anne and our grandchildren,
Daniel, Benjamin, Alexandra, and Jack,
who give us so much pleasure

Foreword

by Professor George A. Olah
Nobel Laureate

Chambers' book *Fluorine in Organic Chemistry* was published 30 years ago and became a classic of the field. A revised and updated edition is a significant and authoritative contribution by one of the leaders of organic fluorine chemistry. Organic fluorine chemistry has grown enormously in significance and scope in the intervening three decades, not in small measure by the contribution of the author and his colleagues. The new edition will be of great value and help not only to those interested in fluorine chemistry, but also to the wider chemical community. When considering a new edition of a 'classic' of chemical literature, it is most appropriate to maintain broadly the layout and aims of the original book, concentrating on methodology, mechanism and the unique chemistry of highly fluorinated compounds. Understandably, therefore, it is outside the scope to discuss medicinal and biochemical aspects. Readers interested in these topics are advised to use the extensive reviews that are available elsewhere.

Preface

This book is a revision and update of one that was first published in 1973, followed by two small reprintings. The original was prompted by Professor George Olah, during a year that I spent as a Visiting Lecturer in Cleveland. My aim for the original edition was to present an overview of organofluorine chemistry, in a way that corresponded with modern organic chemistry. Of course this involved including a mechanistic basis of the subject, which was still evolving at the time; to my knowledge, this was the first broad attempt to do so. The original book appears to have served a useful purpose because, for a number of years now, friends in the field have encouraged me to write an update.

In the intervening years since the first edition the subject has grown enormously, and any idea of a single-author comprehensive volume would now be a preposterous undertaking. Consequently, I have concentrated attention on illustrating the principles of the subject, and especially those concerning highly fluorinated compounds, where the chemistry is quite unusual. Inevitably, important areas are omitted: for example the impact of fluorine as a label in biochemistry, which is outside my expertise. However, I hope that there are enough key references to important areas that I have neglected.

Inevitably, my choice of illustrative examples is subjective and I apologise in advance for all the beautiful examples that have not been included.

The considerable task of producing the manuscript would not have been completed without the continued help of a long-term friend and collaborator, Dr. John Hutchinson, to whom I am deeply indebted. Also, my sincere thanks to the Leverhulme Trust for an Emeritus Fellowship, during the tenure of which the book was written. Thanks also to my colleague, Dr Graham Sandford, for invaluable help and discussions, and to Dr Darren Holling, Rachel Slater and Chris Hargreaves for reading the manuscript. Last, but not least, thanks to my wife Anne for her continued forbearance.

Dick Chambers

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Chapter 1

General Discussion of Organic Fluorine Chemistry

I GENERAL INTRODUCTION

One of the major activities of chemists in industry and academia is the search for ‘special-effect’ chemicals, i.e. systems with new chemistry and with novel properties that can be exploited by industry. There are, of course, many ways of creating novel systems but the introduction of carbon–fluorine bonds into organic compounds has led to spectacular industrial developments, together with an exciting field of organic chemistry and biochemistry.

Fluorine is unique in that it is possible to replace hydrogen by fluorine in organic compounds without gross distortion of the geometry of the system but, surprisingly, compounds containing carbon–fluorine bonds are rare in nature [1, 2]. In principle, therefore, we could introduce carbon–fluorine bonds singly, or multiply, so that there is the potential for a vast extension to organic chemistry, providing that the appropriate methodology can be developed. Consequently, the study of systems containing carbon–fluorine bonds has become a very important area of research and the subject already constitutes a major branch of organic chemistry, while imposing a strenuous test on our fundamental theories and mechanisms. Moreover, as we shall see later in this chapter, the applications of fluorine-containing organic compounds span virtually the whole range of the chemical and life-science industries and it is quite clear that wherever organic chemistry, biochemistry and chemical industry progress, fluorine-containing compounds will have an important role to play.

Surprisingly, this situation is still not reflected in current general textbooks; the reasons can be traced partly to the very rapid growth of the subject, as well as the difficulty that all workers experience in reaching a wider audience. Therefore, it is hoped that this book will help by presenting an outline of fluorine chemistry on a broadly mechanistic basis. This volume stems from an earlier book [3] on the subject; its aim remains to provide an overview through highlighting a variety of topics but with no attempt to provide comprehensive coverage of the literature. Where appropriate, books and reviews will be cited and the author therefore acknowledges the many sources, referred to either here or in the following text, to which this book is intended to be complementary [4–39].

A Properties

Fluorocarbon systems, in general, present no peculiar handling difficulties and the familiar and powerful techniques of isolation, purification and identification in organic

chemistry are applicable in every way. In fact, fluorocarbons themselves are characterised by high thermal stability and, indeed, elemental fluorine is so very reactive because it forms such 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 perfluorocarbon 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 $1/2$ and so nuclear magnetic resonance spectroscopy plays a powerful role in characterisation [40]. Indeed, the only tool that is not easily available for fluorine is the observation of fluorine isotope effects, because the longest-lived isotope is F-18, with a half-life of only 109 minutes [41] although, even with this limitation, applications as a mechanistic probe have been reported [42].

B Historical development

It could be argued that fluorocarbon chemistry began with Moissan in 1890 when he claimed to have isolated tetrafluoromethane from the reaction of fluorine with carbon, but these results were in error [43, 44]. Swarts, a Belgian chemist, began his studies on the preparation of fluorocarbon compounds [45] by exchange reactions around 1890 and for about 25 years from 1900 he was virtually the only worker publishing in the field. He continued until about 1938, and during that time he contributed a great deal in outlining methods of preparation for a large number of partly fluorinated compounds. It was on the foundation of Swarts's work that Midgley and Henne [46] in 1930 were able to apply fluoromethanes and ethanes as refrigerants, and this development gave the subject some financial impetus for progress. Tetrafluoromethane was the first perfluorocarbon to be isolated pure; it was reported in 1926 by Lebeau and Damiens [47] but not properly characterised by them until 1930 [48] and, in the same year, by Ruff and Keim [49]. Swarts made trifluoroacetic acid [50] as early as 1922 and in 1931 reported that the electrolysis of an aqueous solution of the latter gave pure perfluoroethane [51]. Nevertheless, the first liquid perfluorocarbons were not characterised until 1937, when Simons and Block found that mercury promotes reaction between carbon and fluorine [52]; they were able to isolate CF_4 , C_2F_6 , C_3F_8 , C_4F_{10} (two isomers), cyclo- C_6F_{12} and C_6F_{14} .

It was established that these compounds are very thermally and chemically stable and this led to suggestions by Simons that these materials might be resistant to UF_6 , which was found to be the case. There then ensued a period of very rapid development in the synthesis of fluorocarbon materials, the goal being stable lubricants and gaskets for use in the gaseous diffusion plant for concentrating the ^{235}U isotope, using UF_6 . These wartime developments have been published in various collected forms [53–55]. Tetrafluoroethene was obtained by Ruff and Bretschneider in 1933, who decomposed tetrafluoromethane in an electric arc [56] while Locke *et al.* [57] developed a synthesis in 1934, which involved zinc dehalogenation of $\text{CF}_2\text{Cl}-\text{CF}_2\text{Cl}$. Then the formation of polytetrafluoroethene [58] was discovered in 1938 and in the same period chlorotrifluoroethene was found to polymerise to give a very stable inert transparent polymer. The wartime efforts involved development of these and other new materials. Nevertheless, even at the end of the