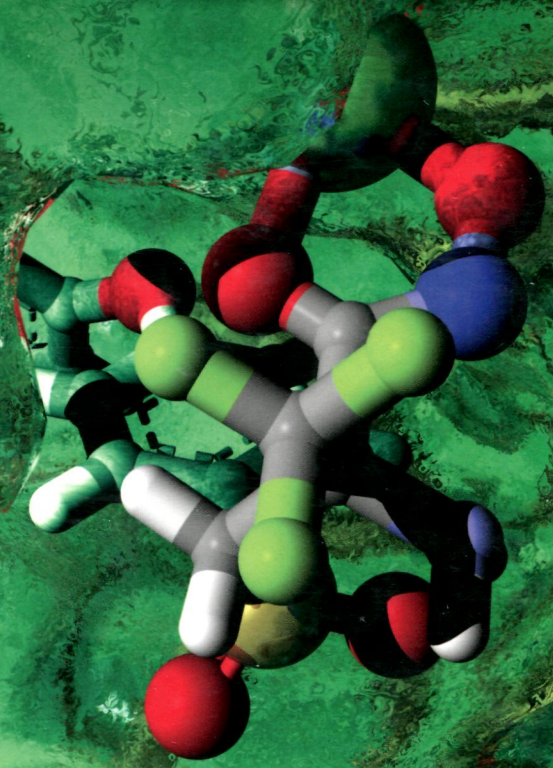
Volume 6

Molecular Medicine and Medicinal Chemistry

# Fluorine in Pharmaceutical and Medicinal Chemistry

## From Biophysical Aspects to Clinical Applications



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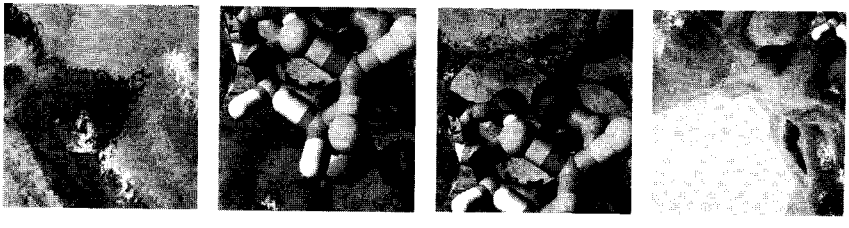


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# Foreword

*François Diederich*

For almost a century after the first preparation of elemental $F_2$ by Moissan in 1886, synthetic fluorine chemistry was pursued and developed by a small community of experts capable of handling the aggressive gas using special laboratory equipment. Important technological developments resulted from this work, such as the bulk-scale preparation of fluorinated hydrocarbons for refrigerators and other cooling devices, which, however, later became banned due to their atmospheric greenhouse effects and the depletion of the ozone layer. Nonetheless, lasting successful applications resulted, for example, from the development of fluorinated polymers such as Teflon®, of volatile gases for anesthesia, and of the separation of uranium isotopes using $UF_6$ centrifuges, for the production of nuclear fuel for use in powerplants.

The development of fluorine-containing drugs started in 1957 and was in the following years strongly aided by the increasing availability of commercial fluorinating agents allowing the safe and selective introduction of organofluorine, i.e. C–F bonds, using common laboratory equipment. This has resulted in the introduction of over 150 fluorinated drugs to the market, and currently nearly 20% of all pharmaceuticals and 40% of all agrochemicals in development contain organofluorine.

The reasons for this explosive growth in interest in the introduction of organofluorine are multiple. While beneficial effects on ADME (absorption, distribution, metabolism, and excretion) and safety were recognized earlier on, the interest in organofluorine has lately focused on more atom-based properties, such as distinct conformational and stereoelectronic properties, modulation of the $pK_a$-value of neighboring

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