

MY FAREWELL TO FLUORINE CHEMISTRY. A BRIEF RESUME OF  
THE PAST AND RECENT RESULTS

M. Hudlický

Department of Chemistry, Virginia Polytechnic Institute and State  
University, Blacksburg, Virginia 24061 (U.S.A.)

Motivated by the discovery of antimetabolic properties of some monofluorinated compounds, I prepared several fluorinated amino acids in the hope that they might have cancerostatic properties. During the syntheses of  $\gamma$ -fluoronorleucine,  $\gamma$ - and  $\delta$ -fluoroisoleucine,  $\gamma$ -fluoroglutamic acid, and especially fluoroaspartic acid, I encountered surprising propensity of fluorine for hydrolytic and hydrogenolytic removal from certain fluoro compounds. Such eliminations occurred when fluorine was intramolecularly nucleophilically displaced by formation of six- and especially five-membered oxygen- or nitrogen-containing rings. Easy elimination of fluorine also took place from  $\beta$ -positions to carboxylic groups, and in certain vicinal bromofluoro compounds such as 2-bromo-3-fluorosuccinic acids. Unexpectedly easy hydrogenolysis of vinylic fluorine was noticed during catalytic hydrogenation of fluoro- and difluorobutenedioic acids. Examples of hydrolytic and hydrogenolytic defluorinations will be discussed.

Avoiding conditions leading to hydrolytic and hydrogenolytic loss of fluorine, I synthesized fluoroaspartic acid [1]. A novel stereospecific synthesis of L-threo- $\gamma$ -fluoroglutamic acid from trans-4-hydroxy-L-proline is outlined below.

