

Preface

There is a substantial didactic difference between retrosynthetic analysis and asymmetric synthesis. This difference refers to the chiral target molecules. They are regarded as racemic in “two-dimensional” retrosynthesis, but one enantiomer is the target in asymmetric synthesis. Retrosynthesis without considering the absolute configuration anticipates the synthesis of racemic target molecules, while asymmetric synthesis leads to the preferred enantiomers. Concerning the conceptual and practical difference between retrosynthesis without consideration of the stereochemistry and asymmetric synthesis of optically pure target molecules, we underline considering asymmetric synthesis as a “departure to the third dimension.”

This book is an attempt to bridge these two aspects of teaching and practicing synthetic organic chemistry. Retrosynthetic analysis is based on the method developed by S. Warren in his monographs as a creative mnemonic tool and a specific departure from the computer-designed multistep syntheses. The attractiveness and pragmatic value of Warren’s approach rest in the adoption of the basic principles of retrosynthetic analysis through application to the problems of the increasing complexity, attaching “computer-like” properties to the brain of synthetic chemists, in particular the capacity to see the target structures in a new, creative way.

The selected examples of asymmetric syntheses in this book are not regularly related to the target molecule of retrosynthetic analysis. Chiral target molecules are selected either to demonstrate the practicability of certain asymmetric syntheses in non-catalytic and catalytic mode, on the laboratory and industrial scale, or because of their scientific originality.

The book characterizes the framework consisting of *chapters* divided into *sections* and preceded by *abstracts* and *introductions*.

Chapter 1 sets the scene by presenting retrosynthetic analysis and a proposal for the synthesis of one simple racemic target molecule, immediately followed by presentation of asymmetric syntheses of one enantiomer of the same target. The aim of this endeavor is to present the substantial difference in the complexity of retrosynthetic analysis of racemates and completing the asymmetric synthesis of the

selected enantiomer to the reader. The following chapters are basically organized around a discussion of the preferred C–C bond disconnections controlled by participation of one or more functional groups. Many aspects of organic reactions are discussed in relation to proposed retrosynthetic steps such as the Diels-Alder cyclization, Birch reduction, Heck reaction, Jones oxidation, Nef reaction, Pfitzner-Moffat oxidation, Pictet-Spengler cyclization, Strecker addition, Suzuki coupling, Wittig condensation and some others. For many important raw materials or building blocks, such as adipic acid, acrolein, *n*- and *iso*-butyric acid, methyl vinyl ketone, cyclohexanone, pyridine, caprolactame, *n*-hexanol, ethyl acetoacetate and phenylacetic acid, a short description of the industrial production method is given. The final chapters are devoted to specific topics, the retrosynthetic approach to heterocyclic structures, rearrangement reactions, retrosyntheses and asymmetric synthesis of complex biologically active compounds. Specific *sections* are devoted to selected topics such as the environmental aspects of organic synthesis, feasibility of the Wittig reaction on the industrial scale, disconnection of the C–C bond correlated to the C–H acidity scale of organic compounds, the Baldwin rules in cyclization reactions, etc. *Examples* are the soul of the book. Most require completion of the retrosynthetic analysis and a proposal for the synthesis. Some of them discuss only synthetic aspects of complex molecules and specific methods of their preparation. *Notes* are inserted into the retrosynthetic discussion and are devoted to a concise description of specific topics, production methods of commodities, explanation of the mechanisms of important reactions, etc.

Nowadays retrosynthetic packages, workshops and retrosynthesis competitions are being developed by collaborations of industry and academy. The authors expect this book to contribute to this trend and bridge retrosynthetic analysis and asymmetric synthesis of chiral target molecules in the optically pure form.

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Synthesis

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