Foreword

E. J. Corey
Nobel Laureate 1990

This book is an enthusiastic celebration of many organic molecules, especially those which are of natural origin, intricate structure and biological relevance. It is also a unique tribute to the many scientists who were involved in their study and chemical synthesis, most of whom are pictured on its pages. Still another element is provided by many interesting historical details and an abundance of colorful illustrations. On top of that, there are innumerable historical vignettes that interweave chemistry and biology in a very appealing way.

Although the emphasis of this work is on chemical synthesis, it contains much that will be of interest to those outside this field and to students of chemistry - indeed to anyone with a fascination with the world of molecules. The authors have selected well over 40 prominent molecules as the key subjects of their essays. Although these represent only a small sample of the world of biologically-related molecules, they amply illustrate the importance of this field of science to humankind and the way in which the field has evolved.

I think that the authors can be confident that there will be many grateful readers who will have gained a broader perspective of the disciplines of chemical synthesis and natural products as a result of their efforts.

E. J. Corey
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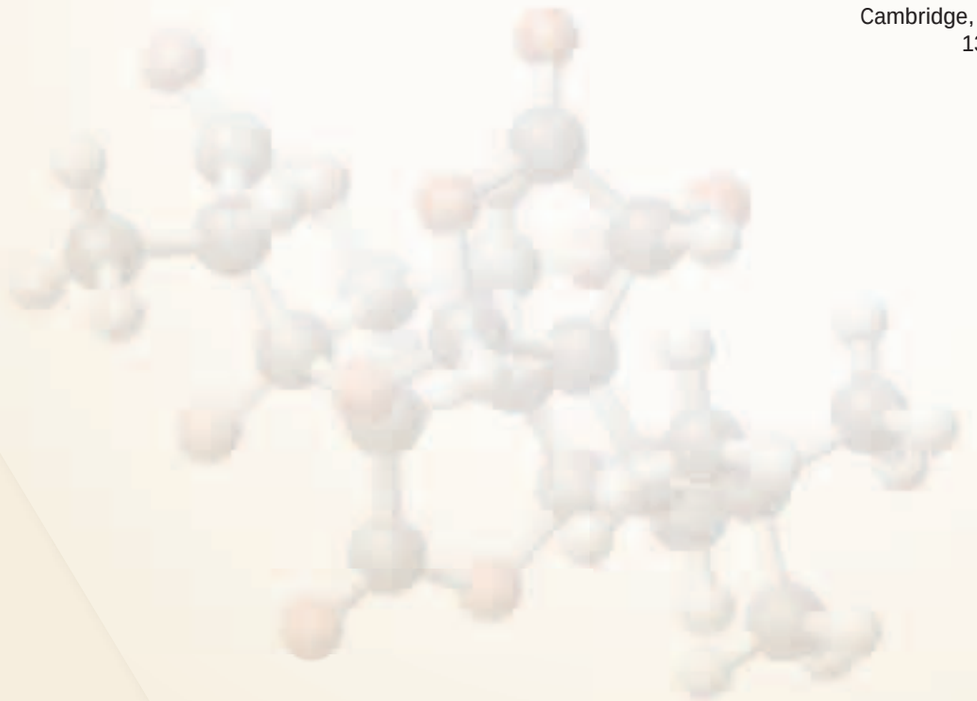
13 August, 2007



Foreword

Ryoji Noyori
Nobel Laureate 2001

Close involvement with society is the destiny of science. Organic Synthesis has been bringing benefits to mankind since the first half of the nineteenth century, longer than almost any other scientific disciplines. *Molecules That Changed the World* has been written to tell the story of this field to future generations. Every chapter abounds with the enthusiasm of the authors, my respected friend Professor K. C. Nicolaou and Dr. T. Montagnon. They convey the intellectual fascination of chemical synthesis, its profundity, its breadth, and its importance as technology, and tell the story in an intriguing and visually appealing way. I believe this book will become a cornerstone of chemistry education.

Chemistry is beyond the science of mere observation and understanding of nature; with Organic Synthesis, we can create high-value substances from abundant natural resources such as oil, coal and biomass. Any molecule is made up of a finite number of atoms connected in accordance with a fixed set of rules. It has a single configuration and may have several conformations. Organic molecules with these precise three-dimensional structures can have amazing properties. Most importantly, we can design any molecule, and if it is sufficiently stable, we can synthesize it by using our accumulated knowledge. So, in principle, we can create molecules that have all kinds of properties. Organic compounds are particularly important in medicine. Many times during the course of human history, small molecules have cured tens of millions of people of serious diseases and improved quality of life. Organic Synthesis will always be the heart of chemistry.

Science is objective. But it is human intelligence and endeavor that discover and create interesting new substances. To date we have discovered or created more than thirty million structurally well-defined compounds. This book selects about forty molecules that have had revolutionary effects and become indispensable for human society. Blending chemistry, biology and medicine, it explains, in simple language, the scientific concepts that are necessary for their chemical synthesis (synthetic methods and path designs) and portrays the pioneering chemists who made the discoveries. The story begins with Friedrich Wöhler's synthesis of urea in 1828, continues through the strategic synthesis of structurally complex bioactive compounds, and concludes with small-molecule drugs and biologics. I am sure that many readers will be impressed and inspired by the colorful history, the beauty of the scientific theories, and the characters of the great scientists featured in this book.

Quo vadis, Organic Synthesis? Where are you going? In the 21st century, chemical synthesis is not just an intellectual challenge but also a vital field for the survival of the human race. Chemists will have to join forces with scientists in other fields, and engineers. One clear direction is for synthetic organic chemistry to merge with the biosciences to create an integrative Science of Life. Living systems all seem very complicated, but they are just collections of large and small organic molecules that function according to the laws

of nature. James Watson, a 1962 Nobel Laureate in Physiology or Medicine, put it well: “Life is simply a matter of chemistry.” When Watson and Crick discovered the double-helix structure of DNA in 1953, it opened the door to molecular biology; the decoding of the human genome, fifty years later, has led to another new world of science. Thanks to advanced technologies and the endeavor of scientists in many fields, we are now able to work out the precise atomic-level structures of large biomolecules such as nucleic acids, proteins, and polysaccharides. This field of Structural Biology has become a part of chemistry—in recent years, several Nobel Chemistry Prizes have been awarded for research in this area as demonstrated in this book.

The focus of chemical research has also been moving from structure to function. Dynamic interactions between large biopolymers and small organic molecules often cause and control processes in living organisms. So Chemical Biology is sure to become even more important. I am confident that in the future scientists will elucidate the chemical mechanisms of cell functions, and even thought and memory.

Organic Synthesis will remain important. But for it to continue being as useful as possible, and maintain its position as a central part of science, chemists will have to understand other fields and collaborate with other scientists. For this we need broader, suitable education. In addition, the significant mission of Organic Synthesis is to produce large quantities of important naturally occurring and artificial compounds, in a straightforward and practical way, and to provide them to society. But synthesis technology is not yet efficient enough for this. We need to develop a range of new catalysis technologies. In particular, Green Chemistry that is beneficial for both the economy and the environment needs to be promoted and supported by the scientific community as well as by governments, industry, and all other sectors of society. And Green Chemistry must not be just a slogan. It must be a “responsible science” that is put into practice to ensure the future of civilized society.

We are proud of our profession. The wonderful achievements of chemical synthesis have largely been made in Europe, America, and Japan, and mostly by men with some notable exceptions, mainly because women were not afforded the same opportunities. I hope that in the 21st century a bigger role will be played by young scientists from the rapidly progressing countries of Asia, and I believe that scientists from different cultural backgrounds and with different values, both men and women, will be able to create molecules that are even more impressive, and make life better for all of mankind. The authors of *Molecules That Changed the World* demonstrate clearly the impact we can have on our own destiny through chemistry. Their book is destined to play a major role in exciting, motivating and educating the next generation of chemists and life scientists from all over the word who are bound to make this dream a reality.

Ryoji Noyori
RIKEN and Nagoya University
Japan
12 September, 2007

Foreword

Anatolia M. Evarkiou-Kaku

As varied as the interests of landmark entrepreneur and scientist Alfred Nobel, *Molecules That Changed the World* explores the story of chemical synthesis by incorporating topics spanning from history and literature to biochemistry and pharmacy. The authors, Professor Nicolaou and Dr. Montagnon, clearly establish dialogue between the cultural background that inspires new discovery and the scientific journey of elucidating the structure and the total synthesis of molecules. For example, the chapter discussing brevetoxin B appealed most to me due to the cultural interconnectedness between the hard science and society; most specifically, I found the relation between biblical phenomena, red tides, and the destructive nature of brevetoxin B captivating. With its clear descriptions and explanations, people of all educational levels can comprehend this book.

For the nonscientist, *Molecules That Changed the World* presents the reader with a background of biochemistry's progress thus far, in addition to an understanding of social, economical, environmental, medical, and research issues the science community faces today. While exposing readers to such sobering issues, the authors convey the material clearly through both written text and colorful illustrations. In these pages, the nonscientist will find interdisciplinary and cross-cultural explanations commingled with science.

For the high school and presumably undergraduate student interested in science, this book ignites a flame of curiosity and excitement. The explanations of molecular structures and process of total synthesis unveil opportunities of research and development for young scientists. The benefits reaped from new discovery and original thinking inspire readers to explore the possibilities. Stressing the importance of forward thinking, this book motivates students and young scientists to plunge into ever-expanding fields of science to overcome new hurdles.

As this captivating book takes readers through history from ancient Greece, Rome, and Asia to today's advancements, we must remember that science will continue to accomplish the unimaginable so long as people continue to submerge their minds in the artistic world of molecules.

Anatolia M. Evarkiou-Kaku
Francis W. Parker School
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San Diego, California
26 July 2007

Preface

Whether you are a high school or college student, post-doctoral fellow, professor, scientist or lay person, you will find a body of enjoyable and useful information within the covers of this book. The chapters within expound upon our learned knowledge of nature's molecules and the ability of man to discover, synthesize, modify and use them to his benefit in ways not formerly envisioned. Through these pages one will also discover just how profound the influence of chemistry is in our daily lives. This book also explores some of the most exciting frontiers of modern science and medicine, and the opportunities they present to young students for future careers. Written and illustrated in a visually distinct and entertaining style, this book aims to provide insight to its readers about the role of chemistry in society in general, and how chemical synthesis, the art and science of constructing natural and designed molecules in particular, shaped and continues to shape our world. Indeed, this volume contains a wealth of information and fascinating tales about molecules and their presence in many goods such as perfumes, dyes, high tech materials, textiles, vitamins, nutritional products, pesticides, insecticides, and, above all, medicines.The history of total synthesis, the flagship of chemical synthesis, as unraveled within serves to admirably explore how chemical synthesis has enabled and facilitated world-shaping innovations since its naissance in 1828.

The inspiration for this book arose from the desire to enlighten and instill a greater appreciation in society at large about a difficult subject – chemistry, and to inspire young students to explore its fascinating, and almost infinite, applications. Many people remember chemistry as one of their most challenging subjects in college, or the class in which they struggled. For others, the mere mention of the word chemistry conjures up images of explosions, poisons, and pollution (toxic waste and dangerous fumes). The reality of chemistry, however, is far more exciting and rewarding, once these unfortunate and distressing images are dispelled. Indeed, beyond this curtain, there lies a beautiful world of molecules with a glorious history and myriad wondrous applications recognized through Nobel Prizes and other awards, prizes that acknowledge brilliant discoveries and magnificent accomplishments whose uses have alleviated untold pain and saved millions of lives. More importantly, the reader will come to greatly appreciate the skills, knowledge, and tools acquired during the campaigns to discover, synthesize, and investigate such wondrous molecules. These emerging technologies are the gift of such endeavors and of their protagonists to humanity, a gift that carries with it the awesome power to shape the pharmaceutical and biotechnology enterprises, petroleum and energy industries, nanotechnology, materials science and technology, agriculture, cosmetics, and even fashion.

Through this treatise we also aspire to capture the imagination of the next generation of students, tantalizing them with the virtues of chemistry, biology and medicine, and the intrigue of the art and science of chemical synthesis. This central discipline is both challenging and rewarding. It demands the best of human character, including a sharp intellect, originality and imagination, dexterity, and stamina. The stories of some of the personalities featured in these pages are also discussed, for they are telling of their genius and dedication. Besides the admiration and respect they deserve, such characters are wonderful role models for young students.

Few other disciplines, if any, impact their adjacent sciences so broadly and decisively as synthesis, for everything we can sense around us is an assemblage of chemicals. The manipulation of these molecules to form new variations is the subject of this science, a discipline that is also a fine art by virtue of its creative nature. However, the power gained through chemistry to shape our surroundings and create new opportunities for humankind comes with responsibilities –continued education, research, and wise application. We hope that this volume will contribute to upholding these duties, help the reader to appreciate the importance of chemistry to our everyday lives, and attract new talent to the ranks of this almost unlimited science. There is so much yet to be discovered and invented by each new generation of synthetic artisans –architects and sculptors– who choose to aim their minds and chisels towards the fashioning of the almost infinite number of yet undiscovered molecules of natural or design origins.

La Jolla — K. C. Nicolaou
September 2007 — Tamsyn Montagnon